

# **ACEIs vs ARBs in management of HTN**

By

Mohammed Kamal Nassar, MD

Lecturer of Nephrology

Mansoura University

# Focus of the Talk

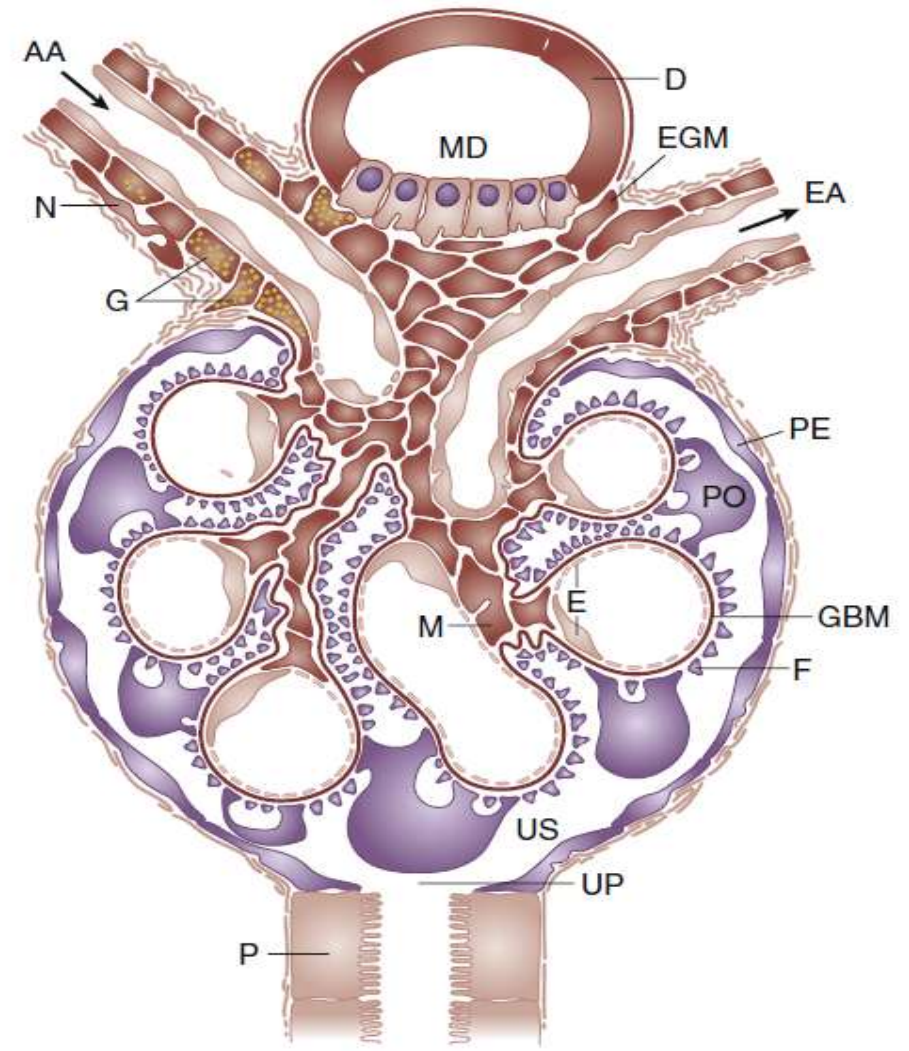
- RAAS
- ACEIs vs ARBs:
  - 1ry Hypertension
  - New onset DM and CV disease
  - Diabetic nephropathy
  - Proteinuria
  - Patients without HF
  - After MI
  - Risk of AF and stroke
  - CV outcomes in PD patients

# Focus of the Talk

- **RAAS**
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## Renin Angiotensin Aldosterone System (RAAS)

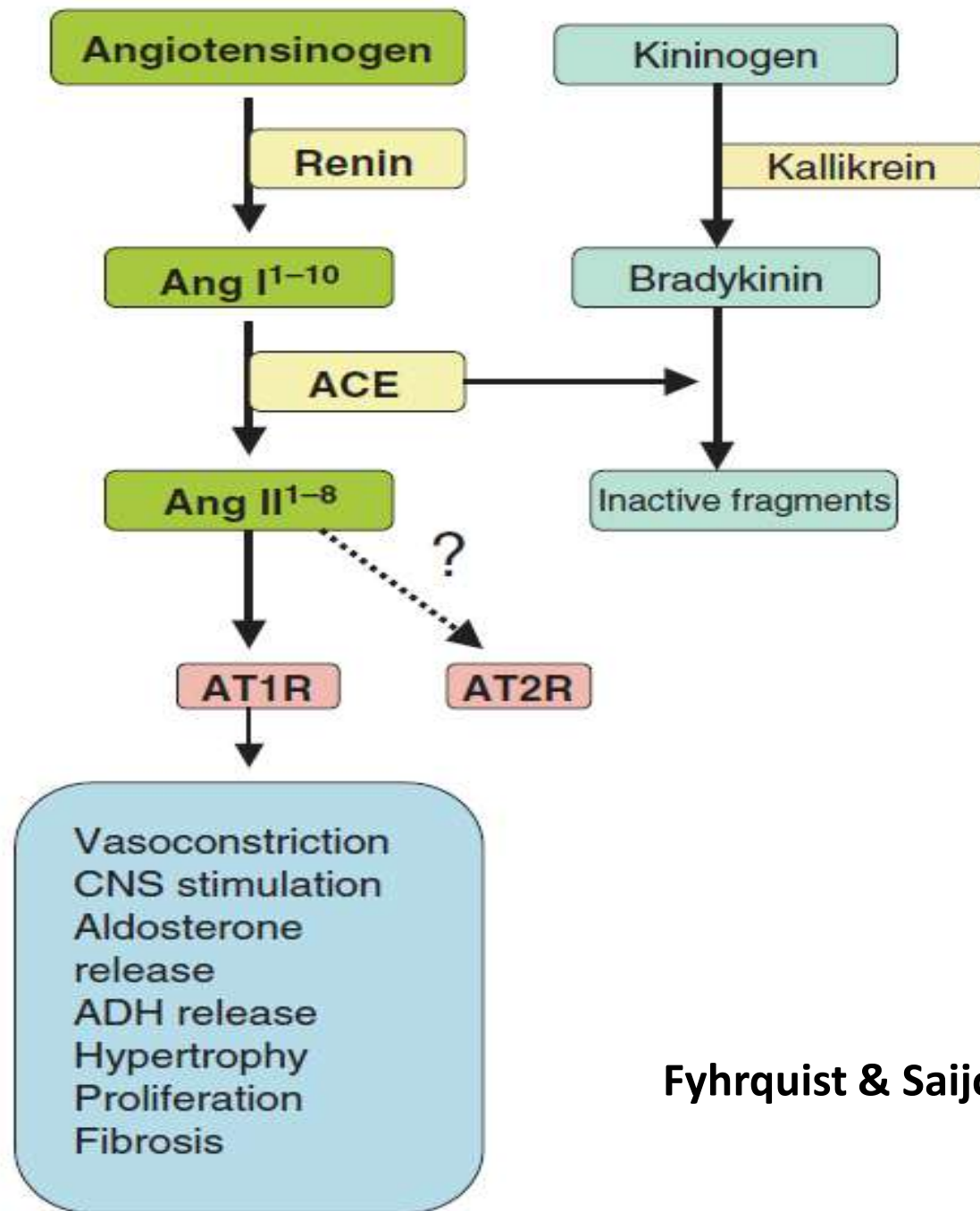
RAAS is central to the control of extracellular fluid volume (ECFV) and blood pressure.



# RAAS - History

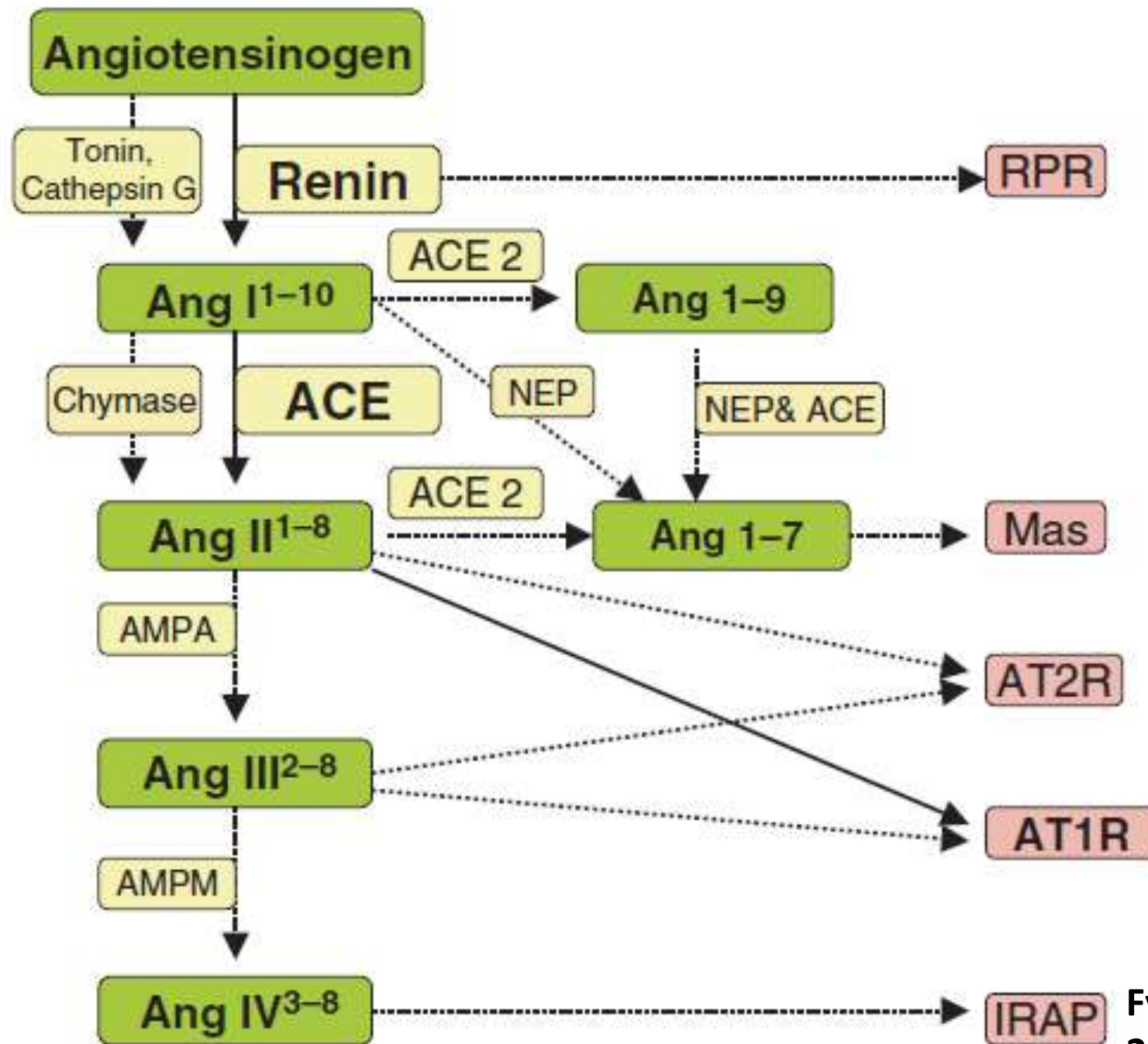
- In 1898, **Tigerstedt and Bergmann** described the prolonged vasopressor effects of crude kidney extracts and named the unidentified active substance “**renin**,” based on its organ of origin.
- in 1934, **Goldblatt and colleagues**: renal ischemia induced by clamping of the renal artery could induce hypertension.
- 1950s:
  - **Skeggs and colleagues** discovered **Ang I and II**.
  - Later, they demonstrated that Ang I was cleaved by “**angiotensin-converting enzyme**,” to generate Ang II.
  - **Laragh, Genest, Davis, Ganong, and their colleagues**, discovered that Ang II also stimulated the release of the adrenal cortical hormone **aldosterone**

# RAAS.....



Fyhrquist & Saijonmaa. J Intern Med 2008; 264: 224–236

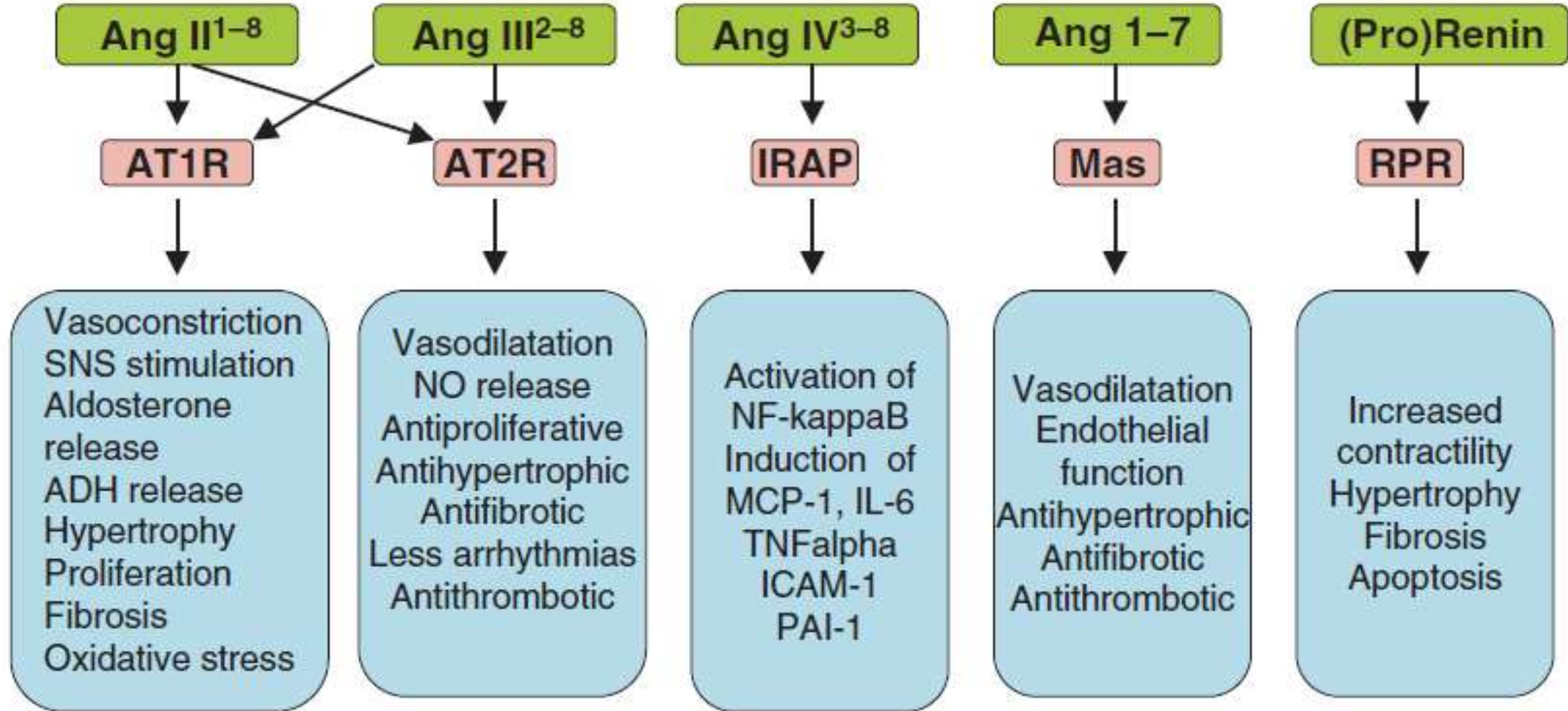
RAAS.....



Fyhrquist & Saijonmaa. J Intern Med 2008; 264: 224–236

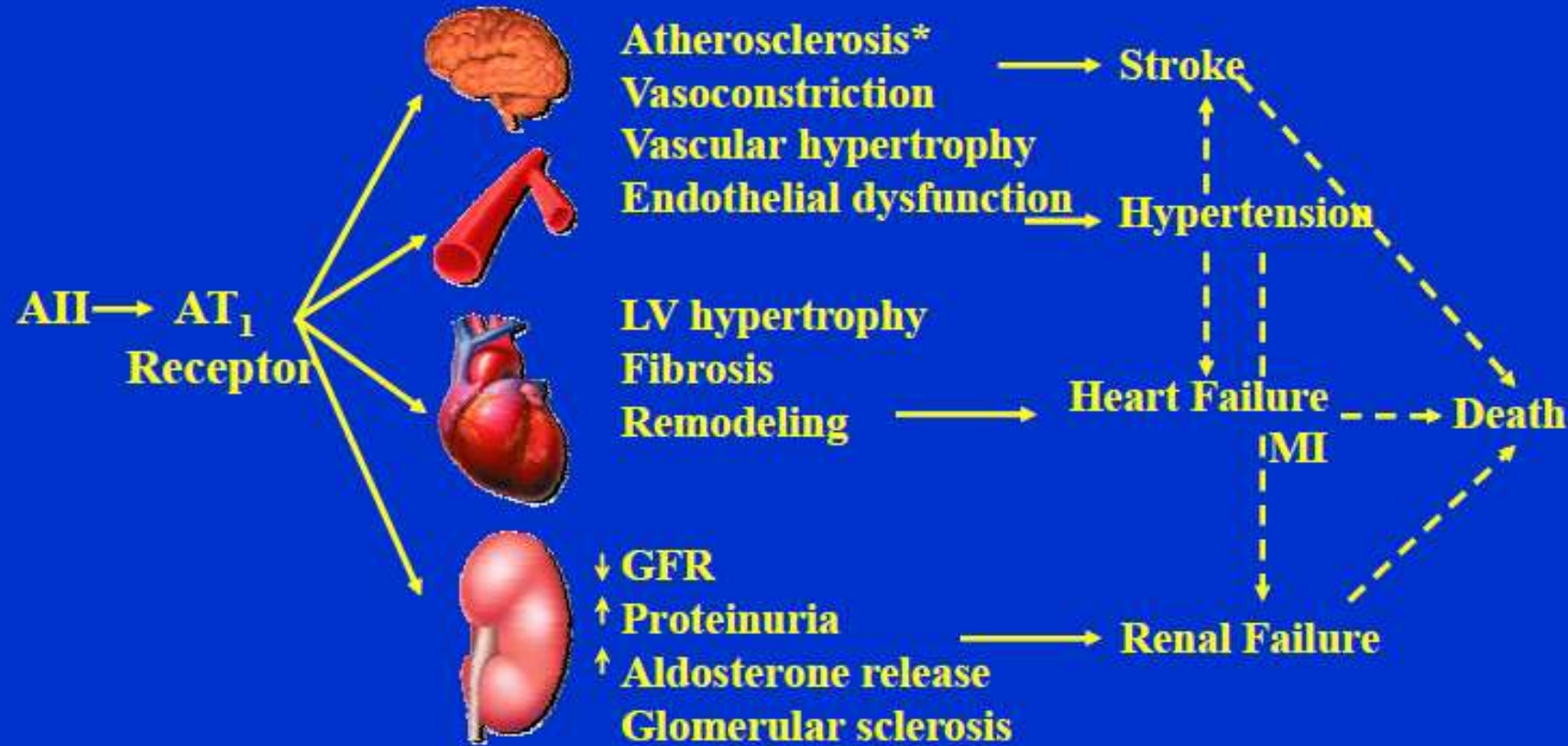


# RAAS.....





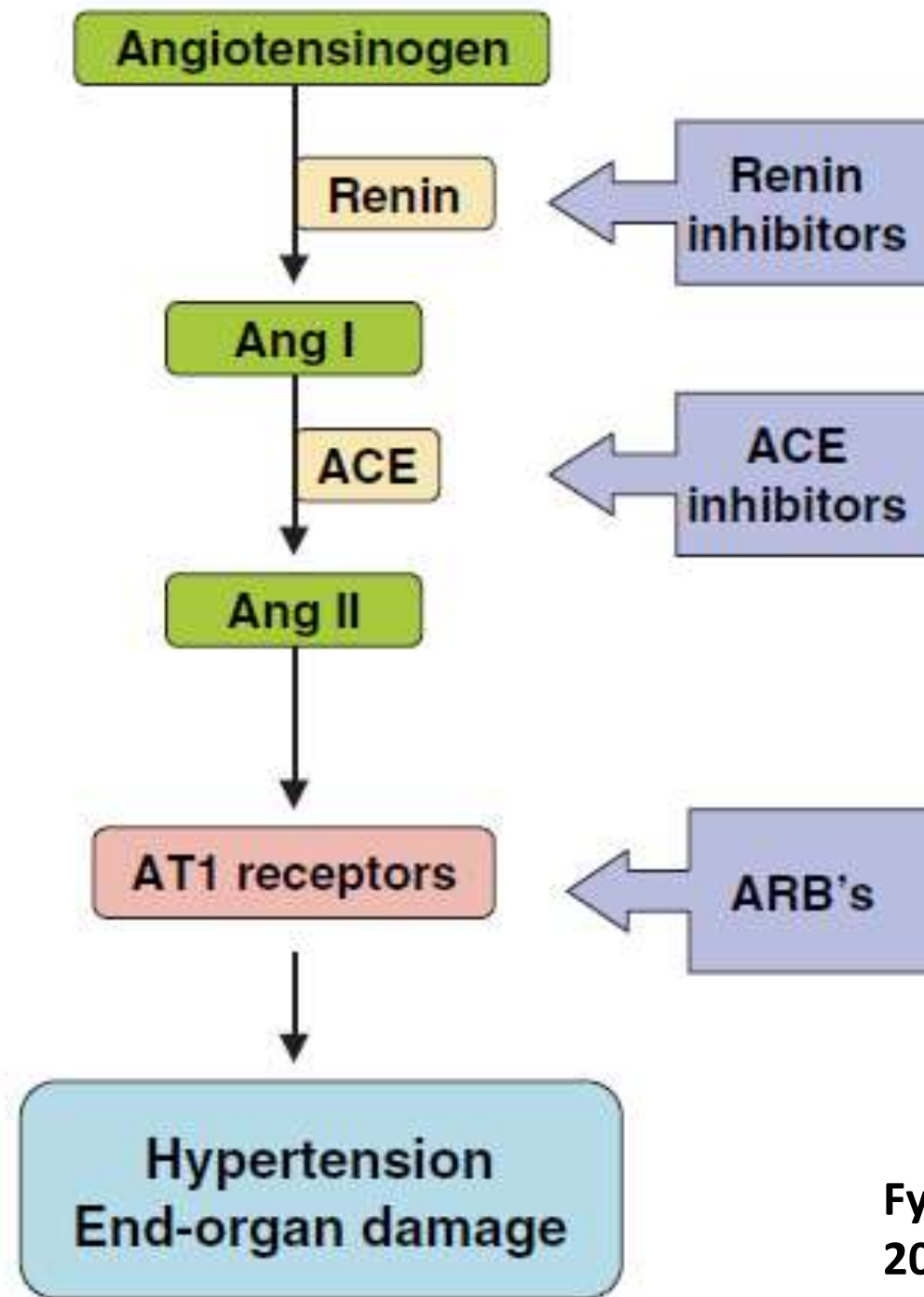
# Angiotensin II Plays a Central Role in Organ Damage



\*Preclinical data.

LV=left ventricular; MI=myocardial infarction; GFR=glomerular filtration rate.

# RAAS.....



Fyhrquist & Saijonmaa. J Intern Med  
2008; 264: 224–236

Drug	Trade name
<b>ACE inhibitors</b>	
Benazepril	Lotensin
Captopril	Capoten Generic
Enalapril	Vasotec
Fosinopril	Monopril
Lisinopril	Prinivil, Zestril
Moexipril	Univasc
Perindopril	Aceon
Quinapril	Accupril
Ramipril	Altace
Trandolapril	Mavik
<b>Angiotensin II receptor antagonists</b>	
Losartan	Cozaar
Valsartan	Diovan
Irbesartan	Avapro
Telmisartan	Micardis
Candesartan	Atacard



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  - After MI
  - Risk of AF and stroke
  - CV outcomes in PD patients

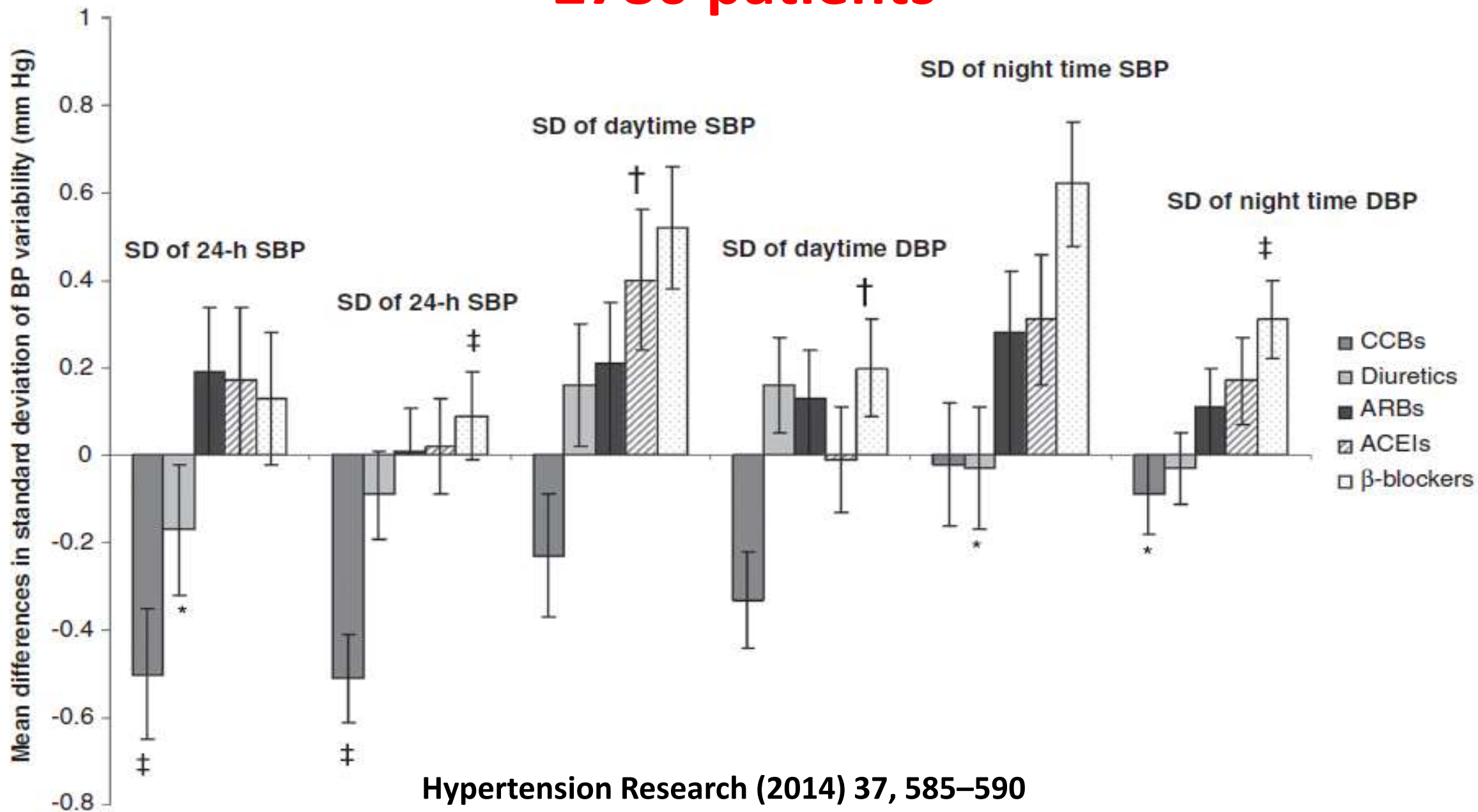
## ORIGINAL ARTICLE

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# Antihypertensive drug classes have different effects on short-term blood pressure variability in essential hypertension

Natacha Levi-Marpillat<sup>1,2,3</sup>, Isabelle Macquin-Mavier<sup>1,2</sup>, Anne-Isabelle Tropeano<sup>4</sup>, Gianfranco Parati<sup>5,6</sup> and Patrick Maison<sup>1,2,3</sup>

2780 patients





# 1ry HTN



**Cochrane  
Library**

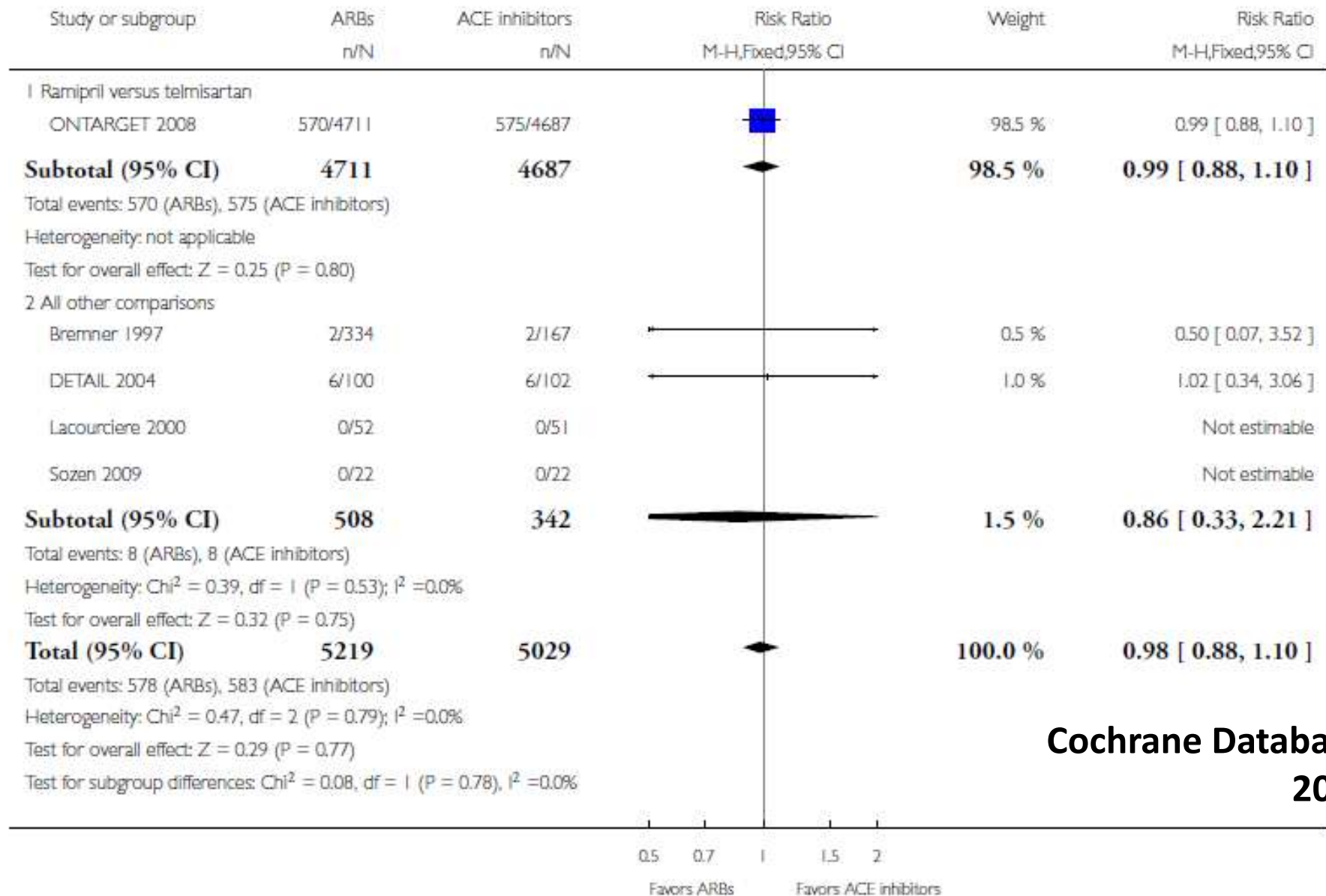
Cochrane Database of Systematic Reviews

[Intervention Review]

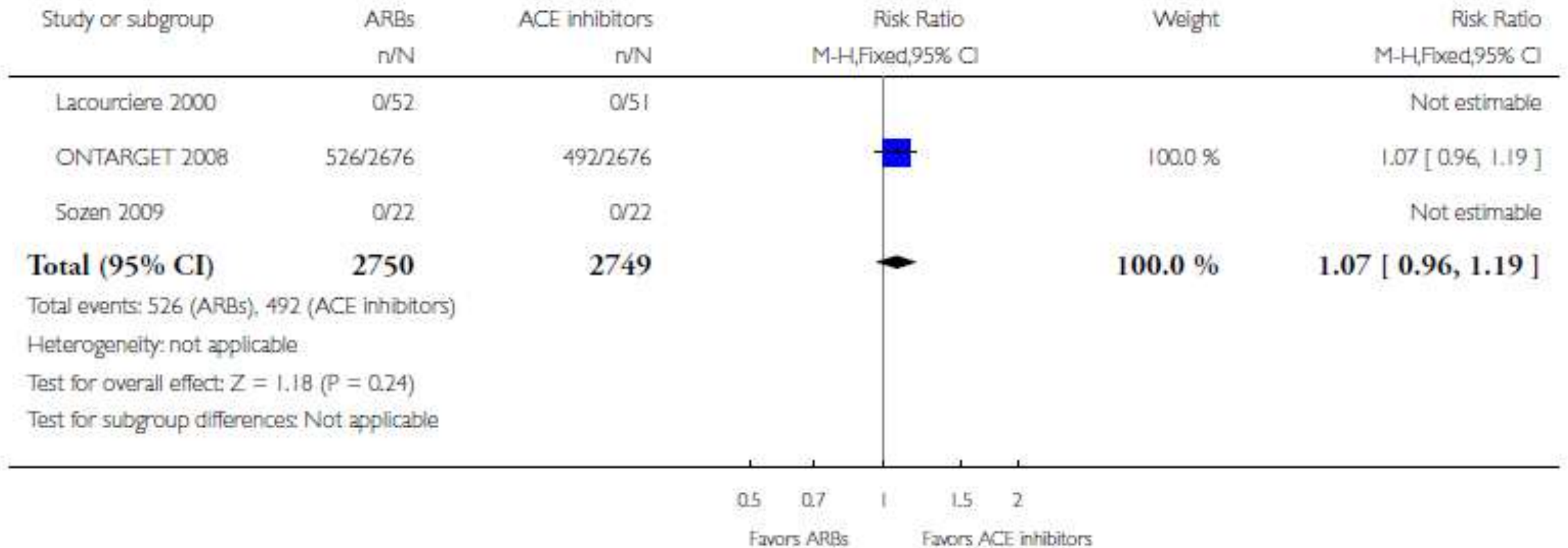
## **Angiotensin converting enzyme (ACE) inhibitors versus angiotensin receptor blockers for primary hypertension**

Edmond CK Li<sup>1</sup>, Balraj S Heran<sup>2</sup>, James M Wright<sup>2</sup>

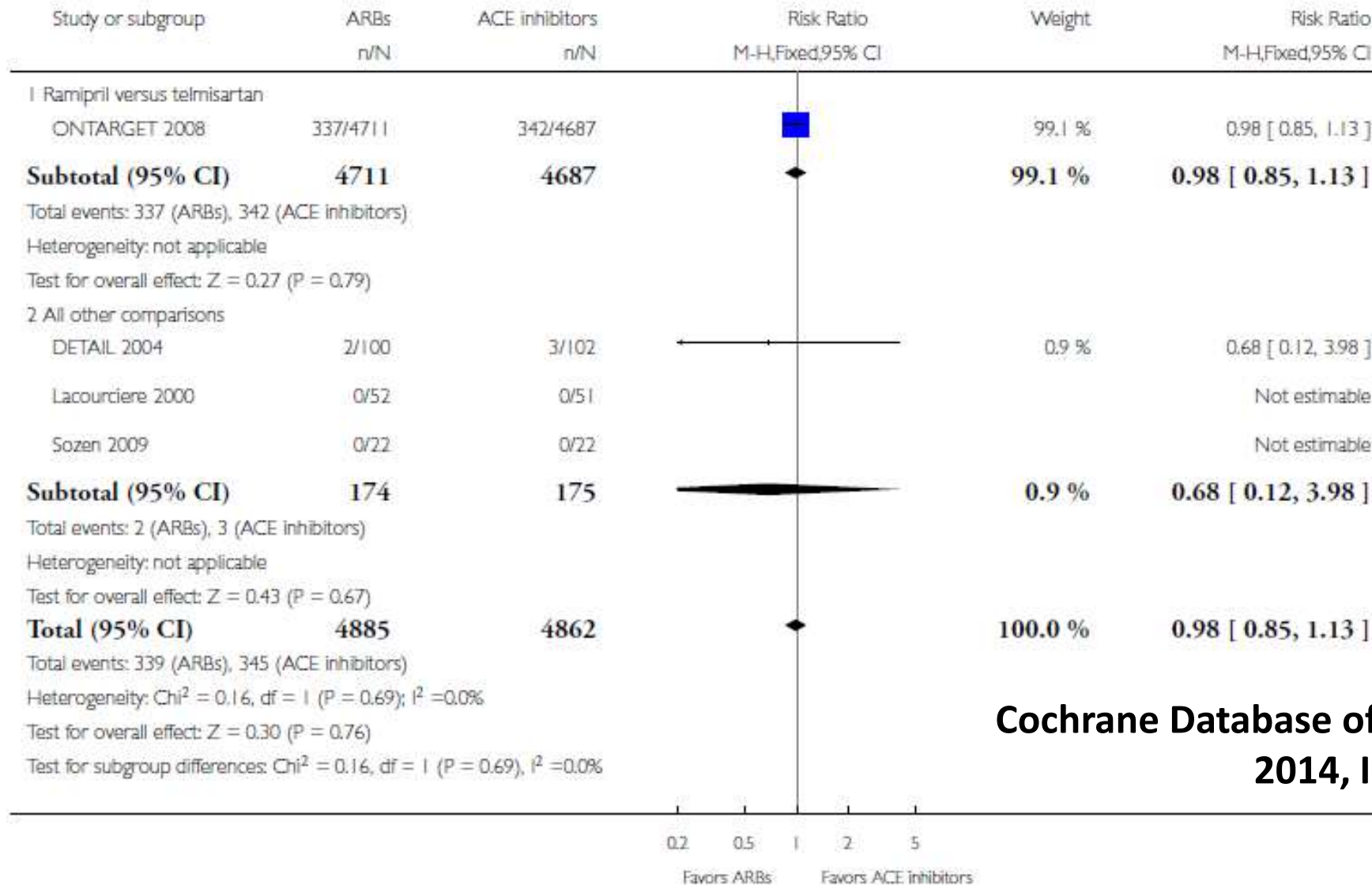
# Total mortality



# Total cardiovascular events

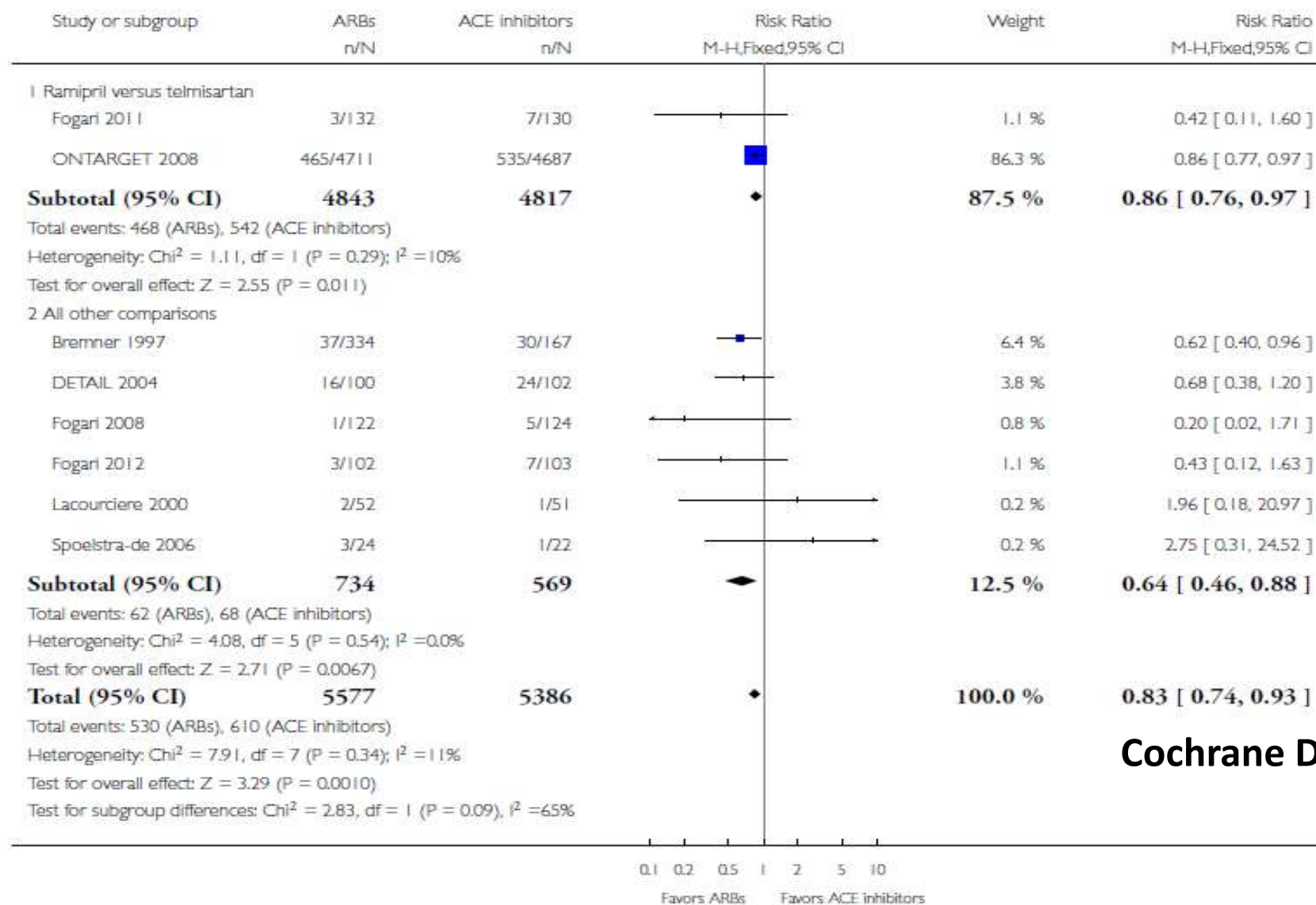


# Cardiovascular mortality



Cochrane Database of Systematic Reviews  
2014, Issue 8

# Withdrawal due to adverse effects



Cochrane Database of Systematic Reviews  
2014, Issue 8

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# New onset DM and CV disease

OPEN

Journal of Human Hypertension (2014) **28**, 663–669

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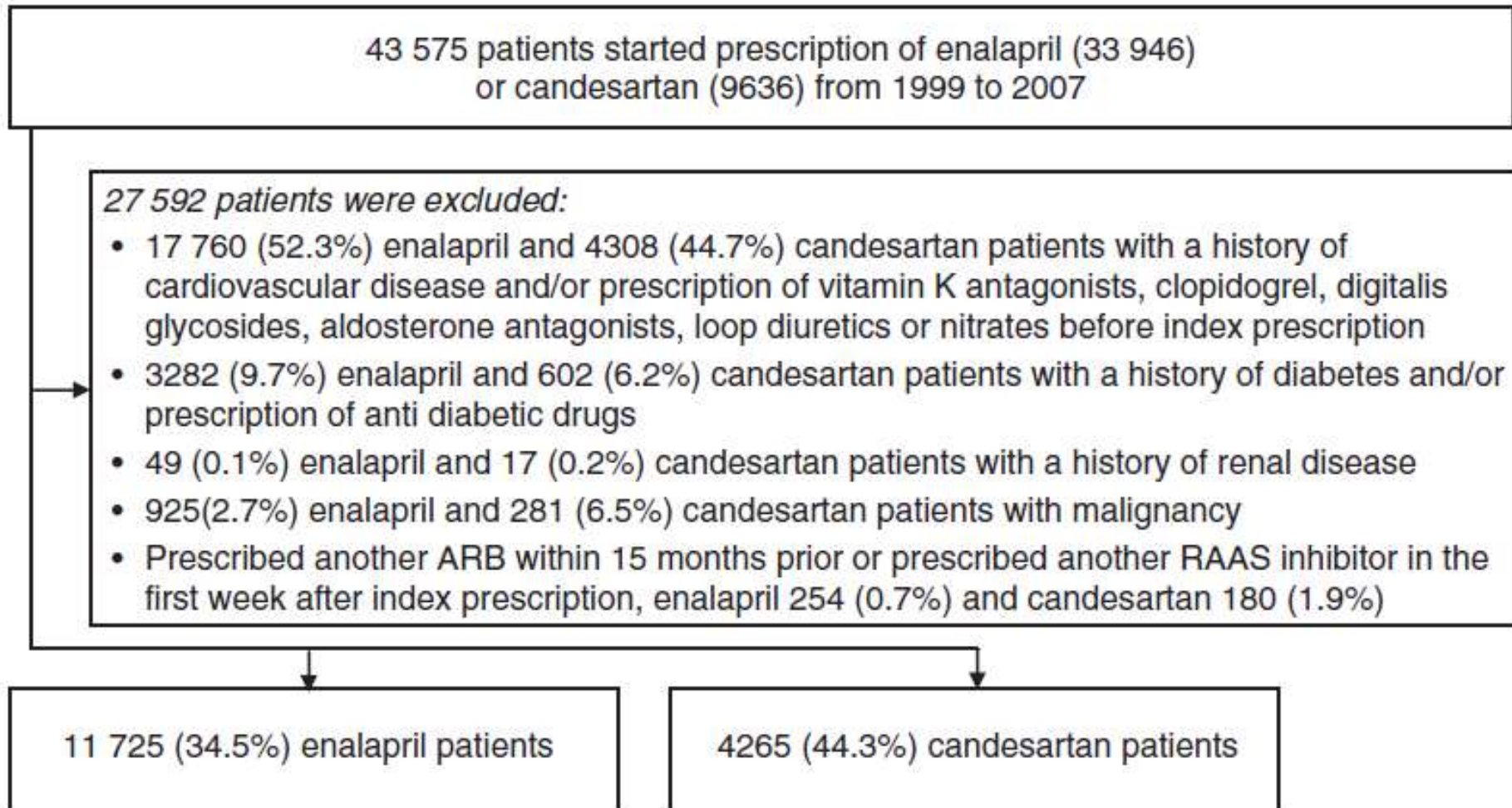


[www.nature.com/jhh](http://www.nature.com/jhh)

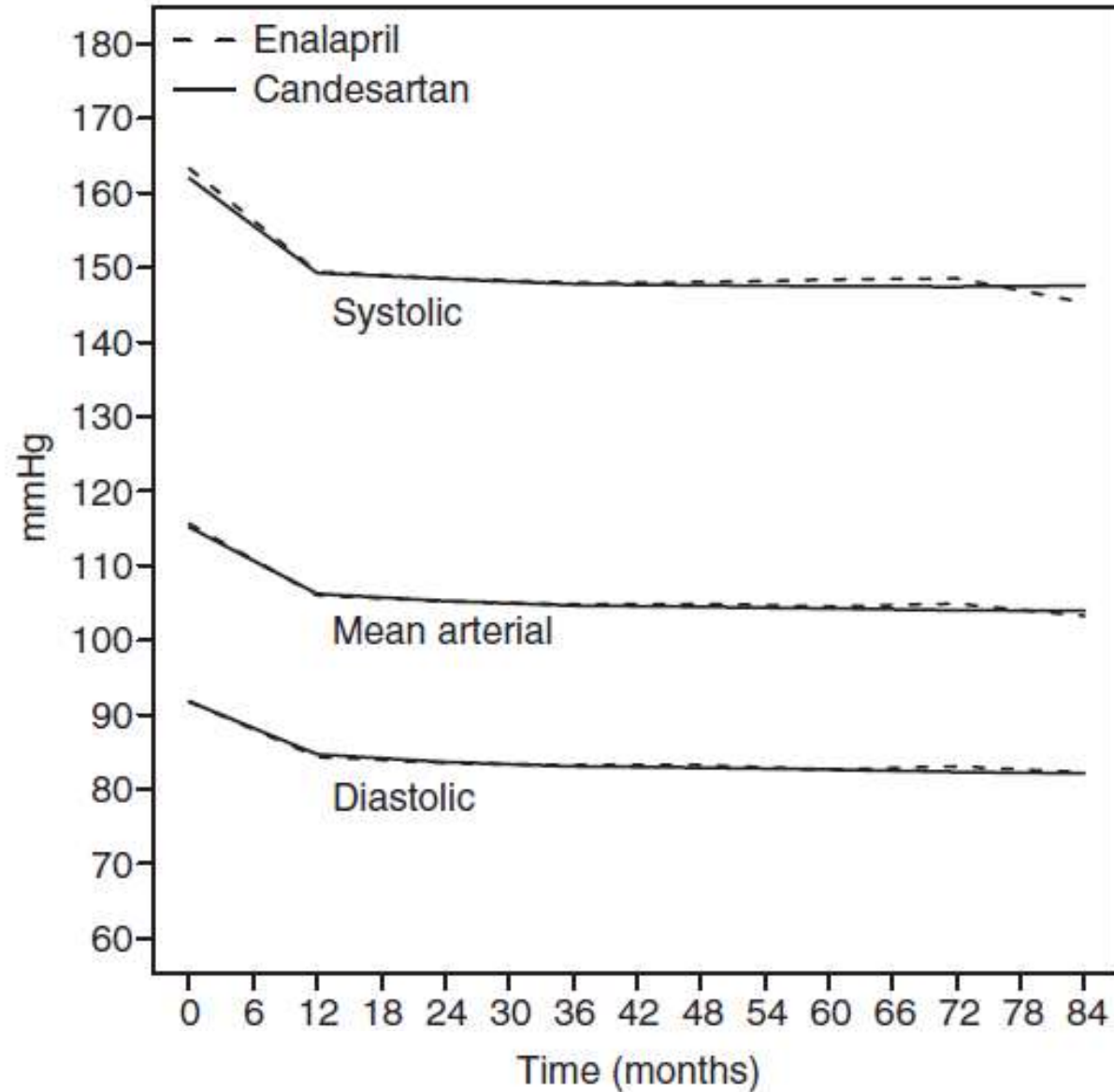
## ORIGINAL ARTICLE

Diabetes and CVD risk during angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker treatment in hypertension: a study of 15 990 patients

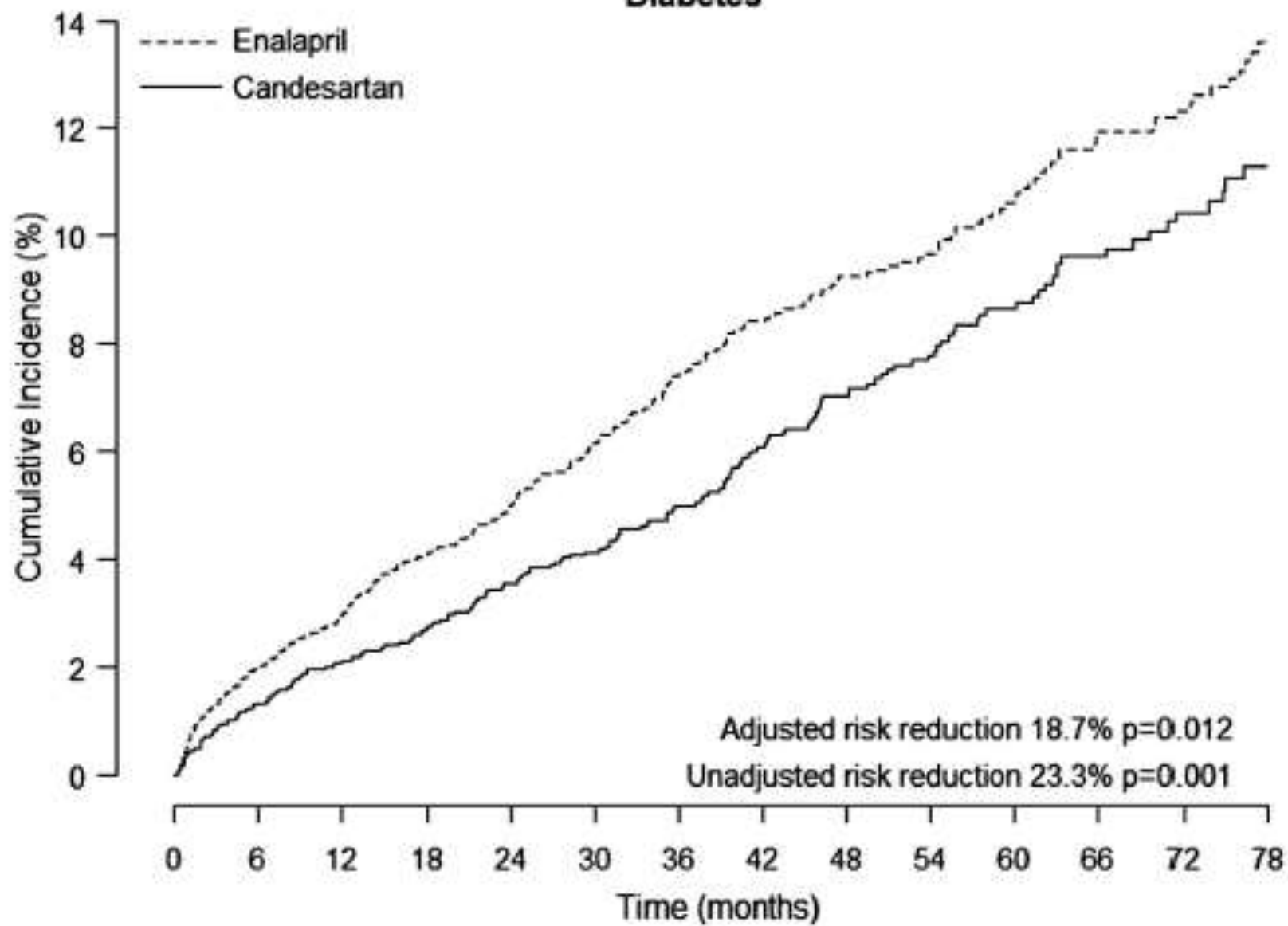
LP Hasvold<sup>1,2</sup>, J Bodegård<sup>2,3</sup>, M Thuresson<sup>4</sup>, J Ståhlhammar<sup>5</sup>, N Hammar<sup>6,7</sup>, J Sundström<sup>8</sup>, D Russell<sup>9</sup> and SE Kjeldsen<sup>10</sup>



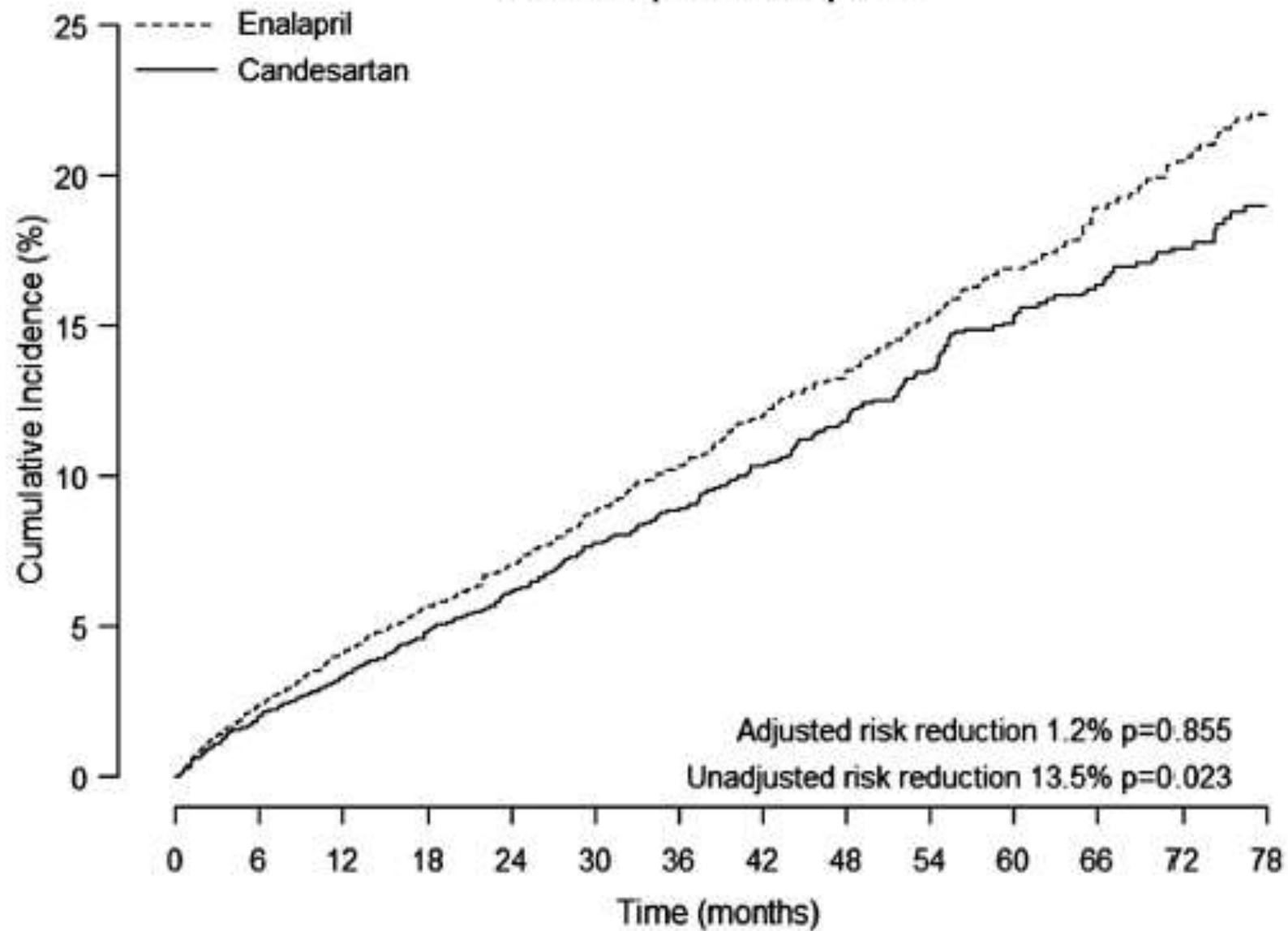
# Blood Pressure



## Diabetes



### CVD composite endpoint



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# Diabetic nephropathy

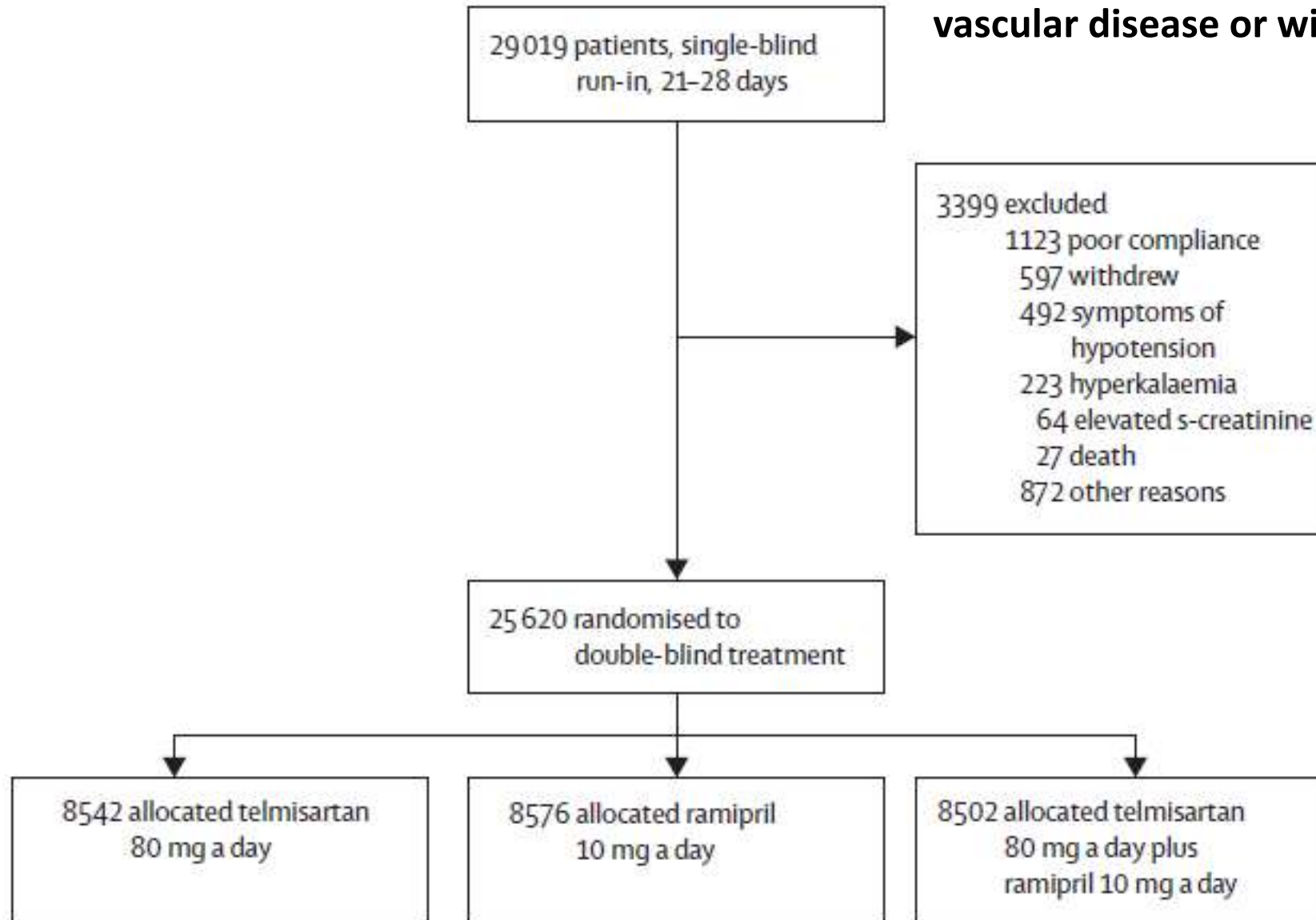
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Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study):  
a multicentre, randomised, double-blind, controlled trial



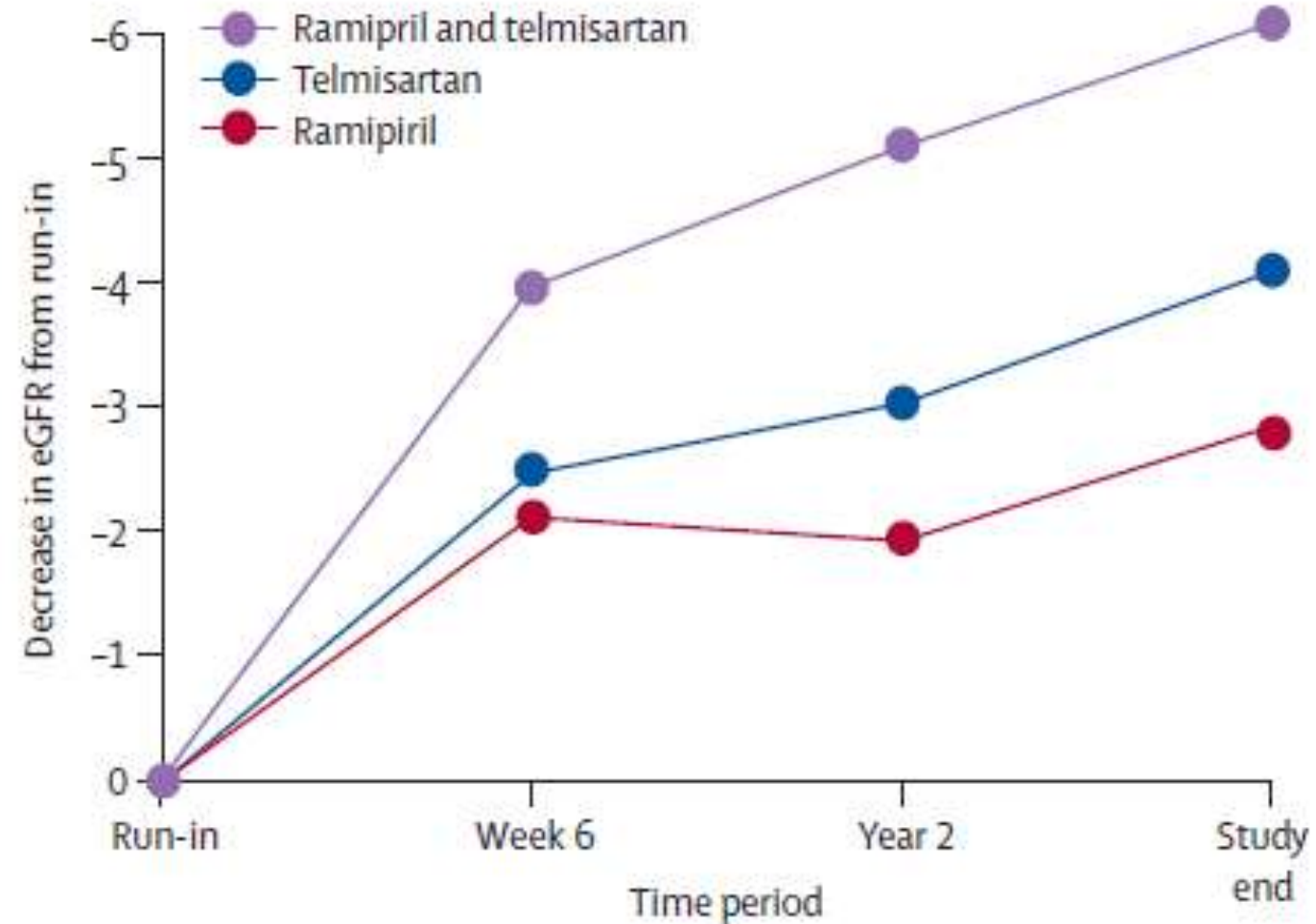
*Johannes F E Mann, Roland E Schmieder, Matthew McQueen, Leanne Dyal, Helmut Schumacher, Janice Pogue, Xingyu Wang, Aldo Maggioni, Andrzej Budaj, Suphachai Chaithiraphan, Kenneth Dickstein, Matyas Keltai, Kaj Metsärinne, Ali Oto, Alexander Parkhomenko, Leopoldo S Piegas, Tage L Svendsen, Koon K Teo, Salim Yusuf, on behalf of the ONTARGET investigators*

**Aged 55 years or older with established atherosclerotic vascular disease or with diabetes with endorgan damage**



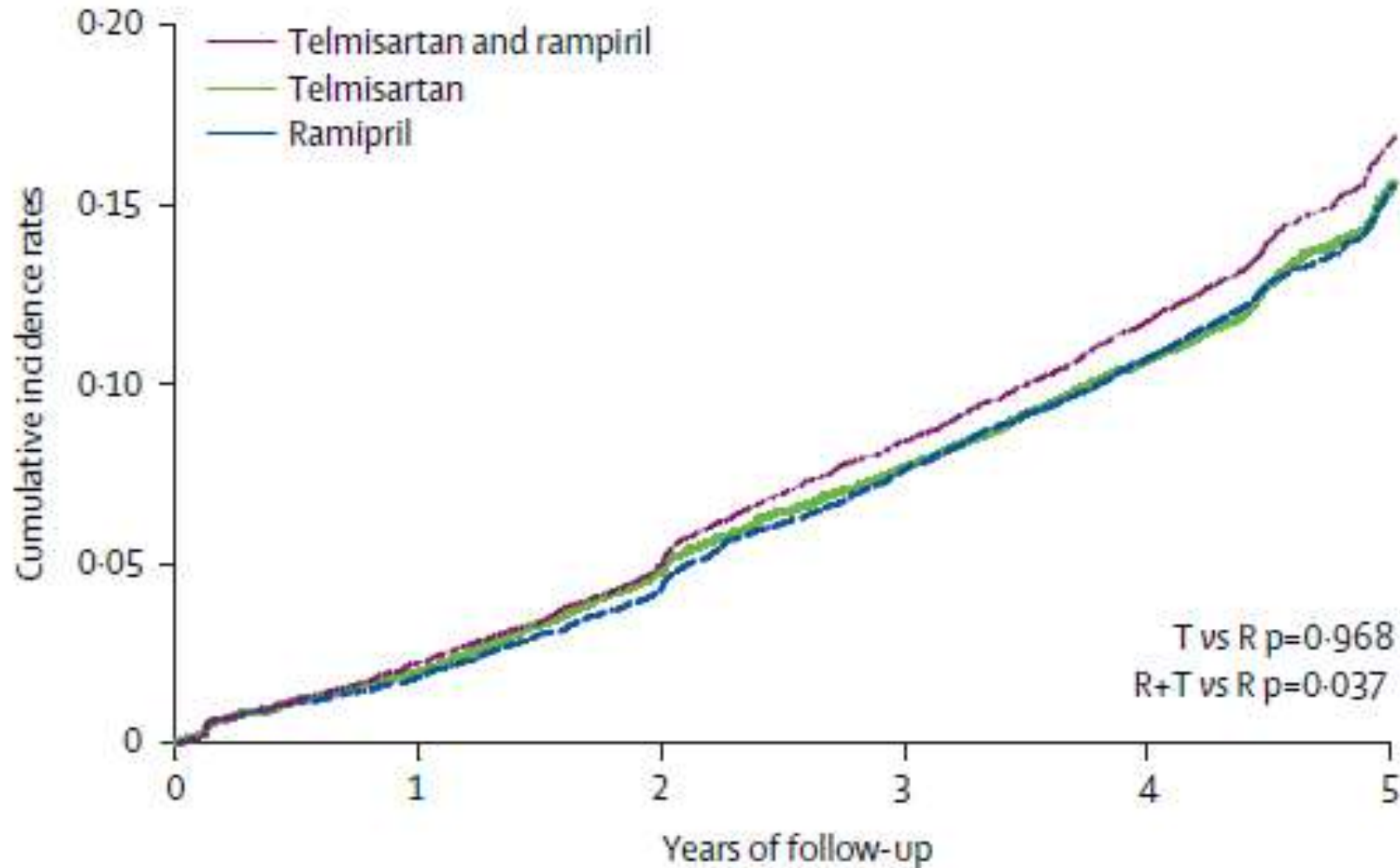
***Lancet* 2008; 372: 547–53**

# Decrease in eGFR



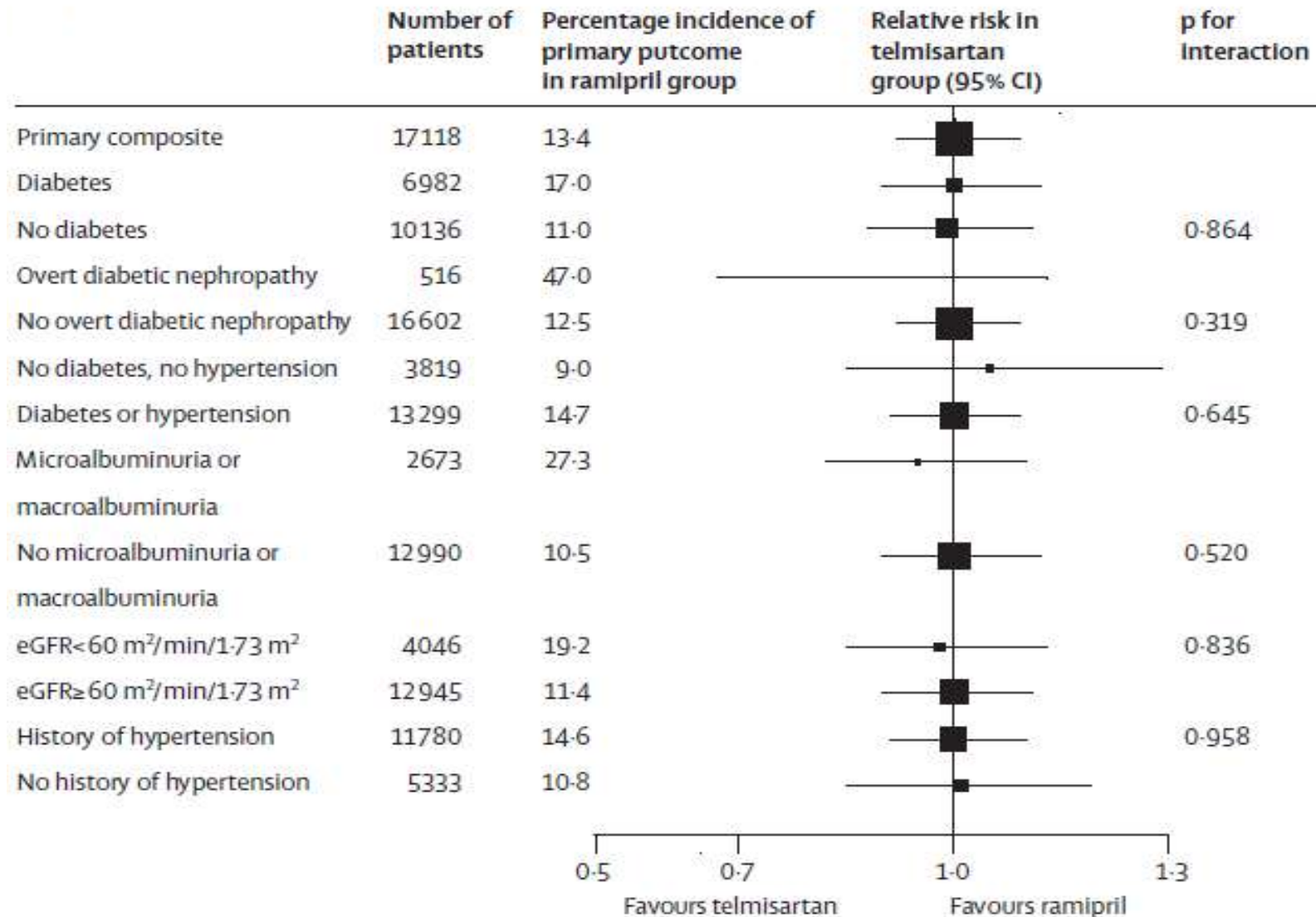
*Lancet* 2008; 372: 547–53

# Dialysis, doubling of serum creatinine, and death



*Lancet* 2008; 372: 547–53

# Dialysis, doubling of serum creatinine, and death



# Diabetic nephropathy

Kidney  
& Blood Pressure  
Research

## Original Paper

Kidney Blood Press Res 297  
DOI: 10.1159/000XXXXXX

Received: April 14, 2009  
Accepted: July 7, 2009  
Published online: ■■■

### Study of ACEI versus ARB in Managing Hypertensive Overt Diabetic Nephropathy: Long-Term Analysis for Results

Savas Ozturk<sup>a</sup> Fuat Sar<sup>b</sup> Olcay Bengi-Bozkurt<sup>b</sup> Rumeyza Kazancioglu<sup>a</sup>

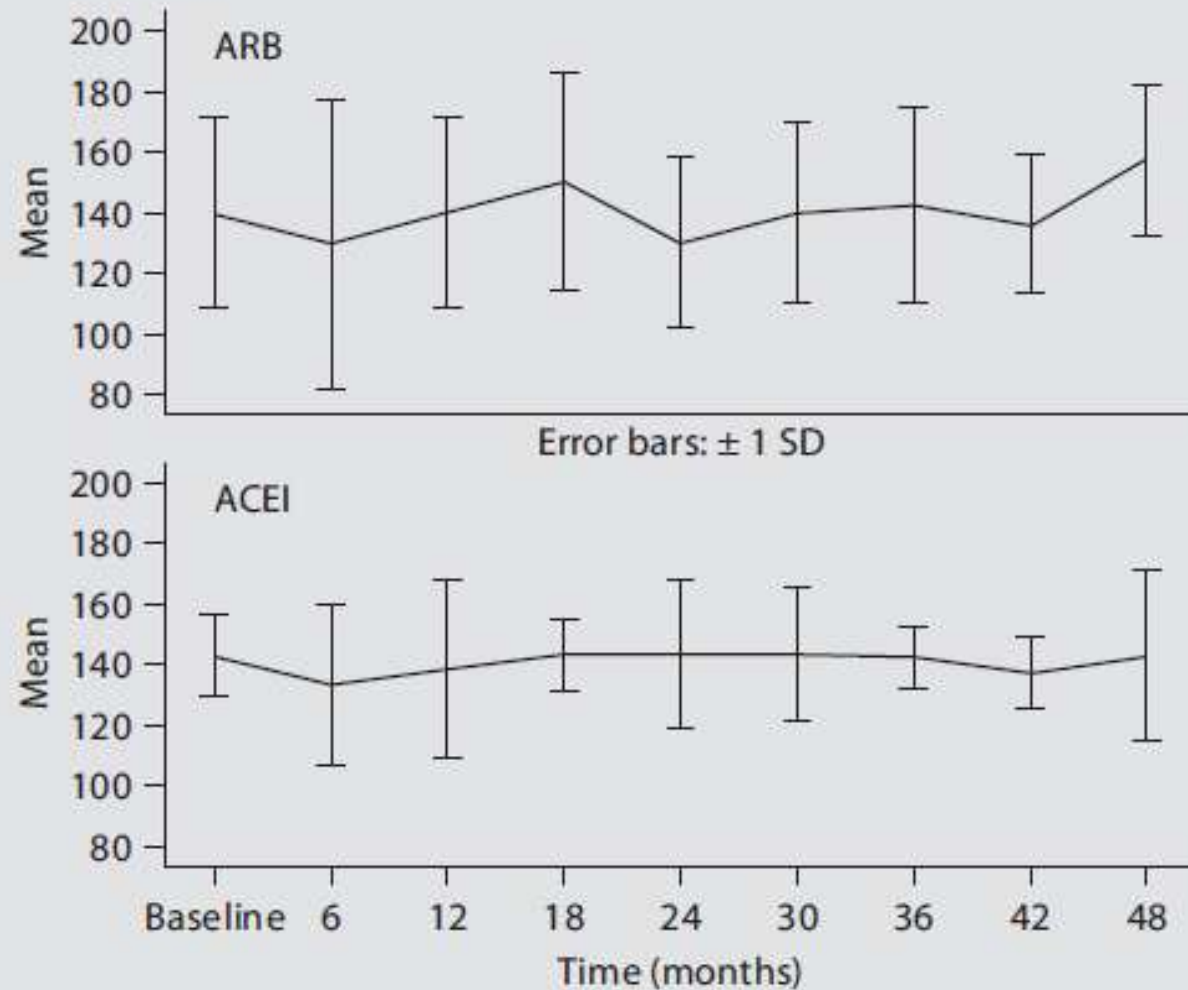
Department of <sup>a</sup>Nephrology and <sup>b</sup>Internal Medicine, Haseki Training and Research Hospital, Istanbul, Turkey

**100 DM and HTN with with GFR < 90 ml/min:**

- 59 patients: ACEIs
- 41 patients: ARBs

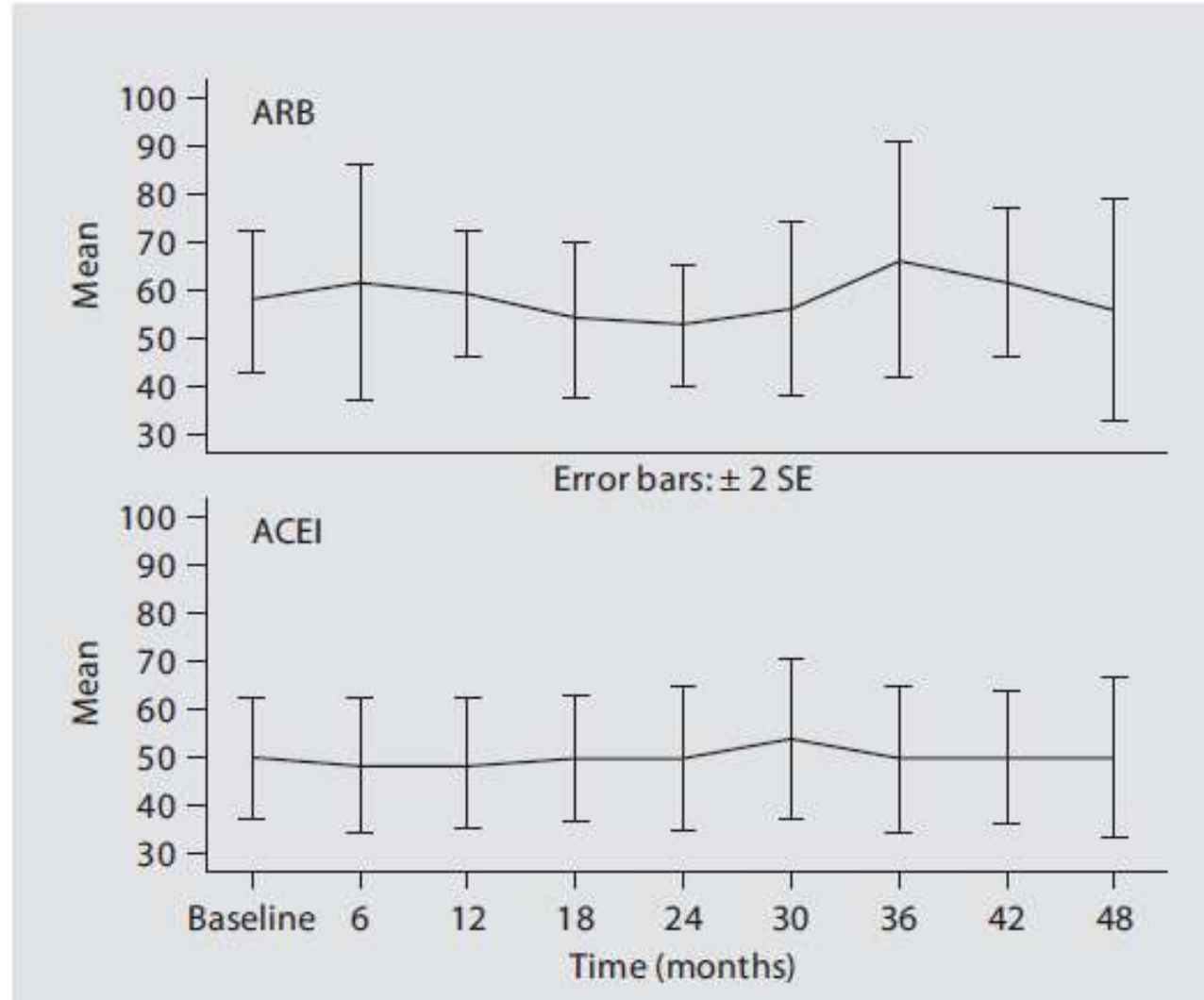


# Changes in SBP



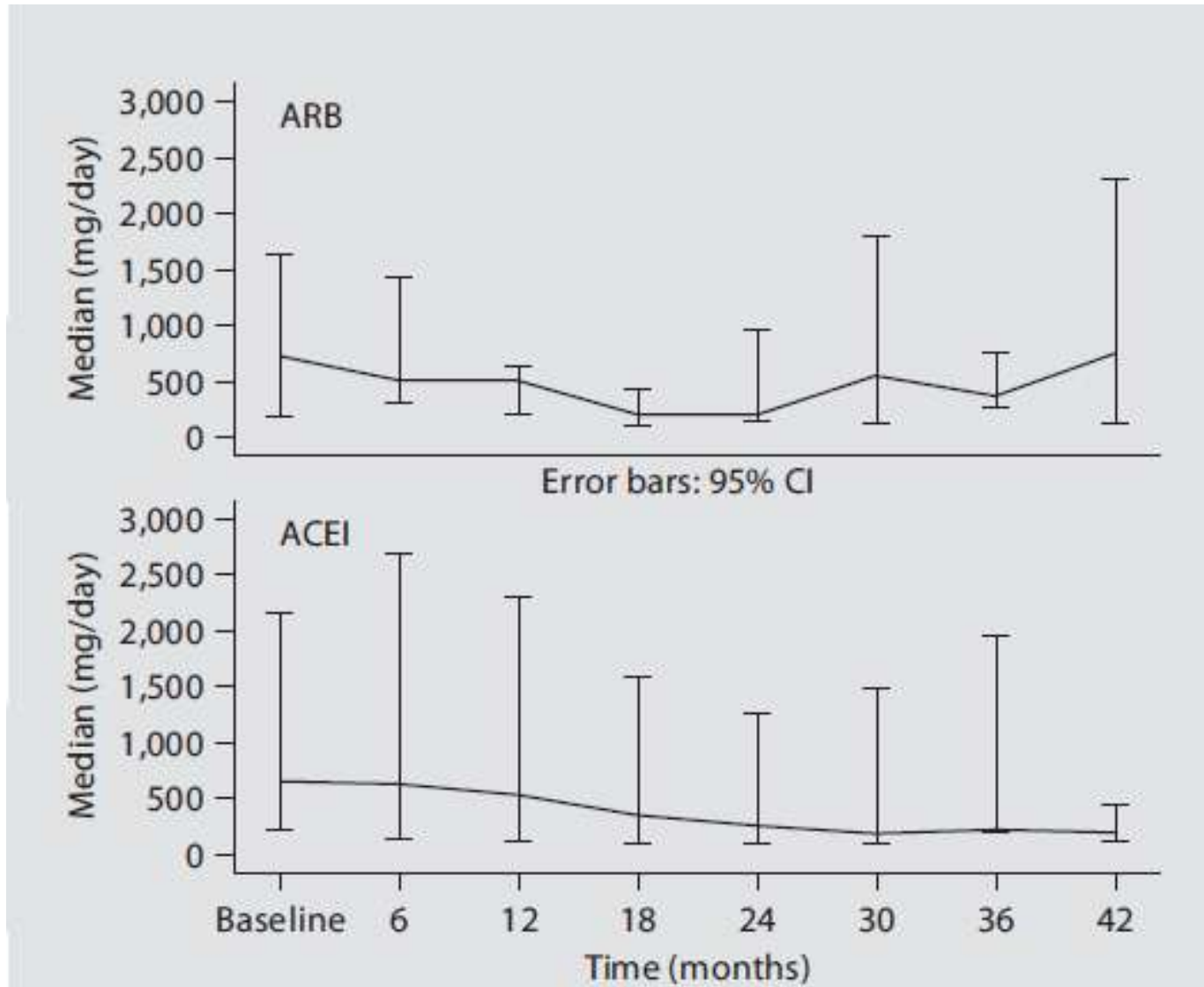
**Kidney Blood Press Res 2009**

# Changes in CC (ml/min)



**Kidney Blood Press Res 2009**

# Changes in proteinuria



**Kidney Blood Press Res 2009**

# Conclusion

ACEIs and ARBs have similar outcomes in overt DNP. Their renoprotective effects can be observed in spite of uncontrolled hypertension.

**Kidney Blood Press Res 2009**

# ACEIs or ARBs in DN !!!!!!!

Nephrol Dial Transplant (2015) 30: ii1–ii142  
doi: 10.1093/ndt/gfv100



## *Clinical Practice Guideline*

Clinical Practice Guideline on management of patients  
with diabetes and chronic kidney disease stage 3b  
or higher (eGFR <45 mL/min)

Clinical Practice Guideline on management of patients with diabetes and chronic kidney disease stage 3b or higher (eGFR <45 mL/min)

## Statements

- 3.2.1 We recommend that adults with CKD stage 3b or higher (eGFR <45 mL/min/1.73 m<sup>2</sup> or on dialysis) and diabetes who have a cardiovascular indication (heart failure, ischaemic heart disease) be treated with an ACE-I at maximally tolerated dose (1B).

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# Proteinuria

Medicine<sup>®</sup>

SYSTEMATIC REVIEW AND META-ANALYSIS

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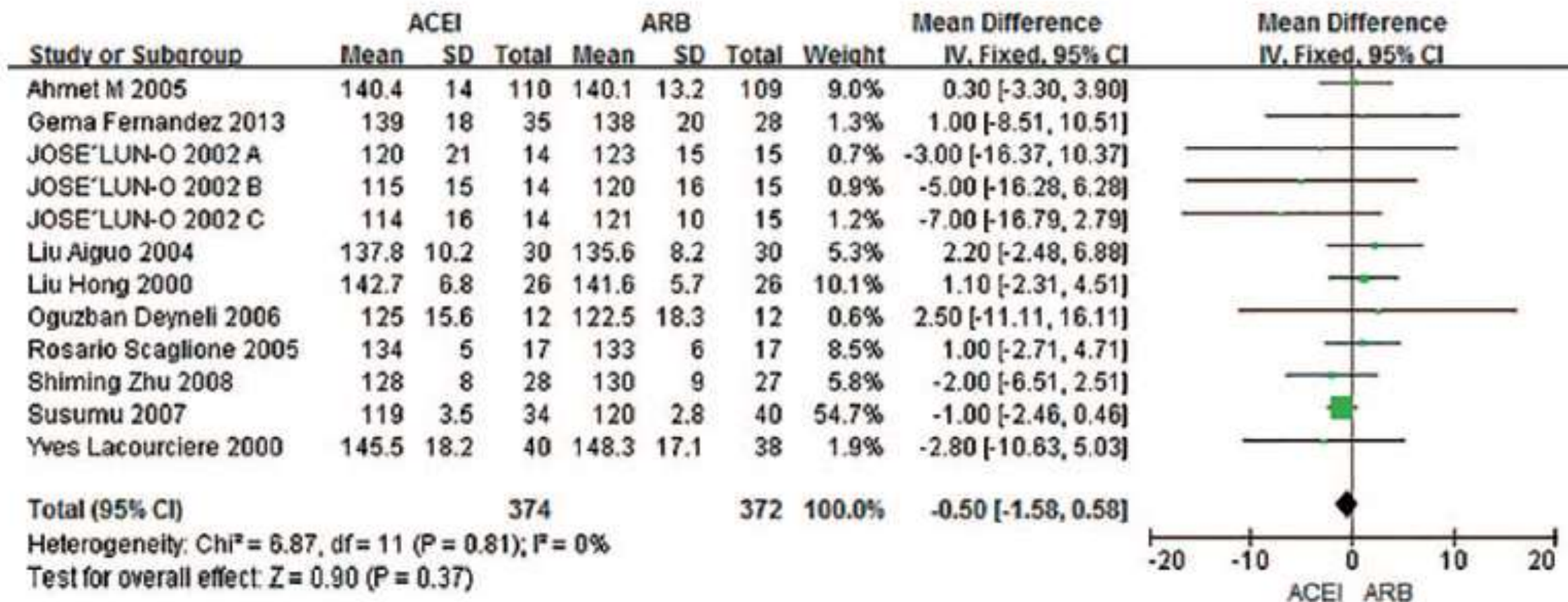
## Effects of ACEIs Versus ARBs on Proteinuria or Albuminuria in Primary Hypertension

*A Meta-Analysis of Randomized Trials*

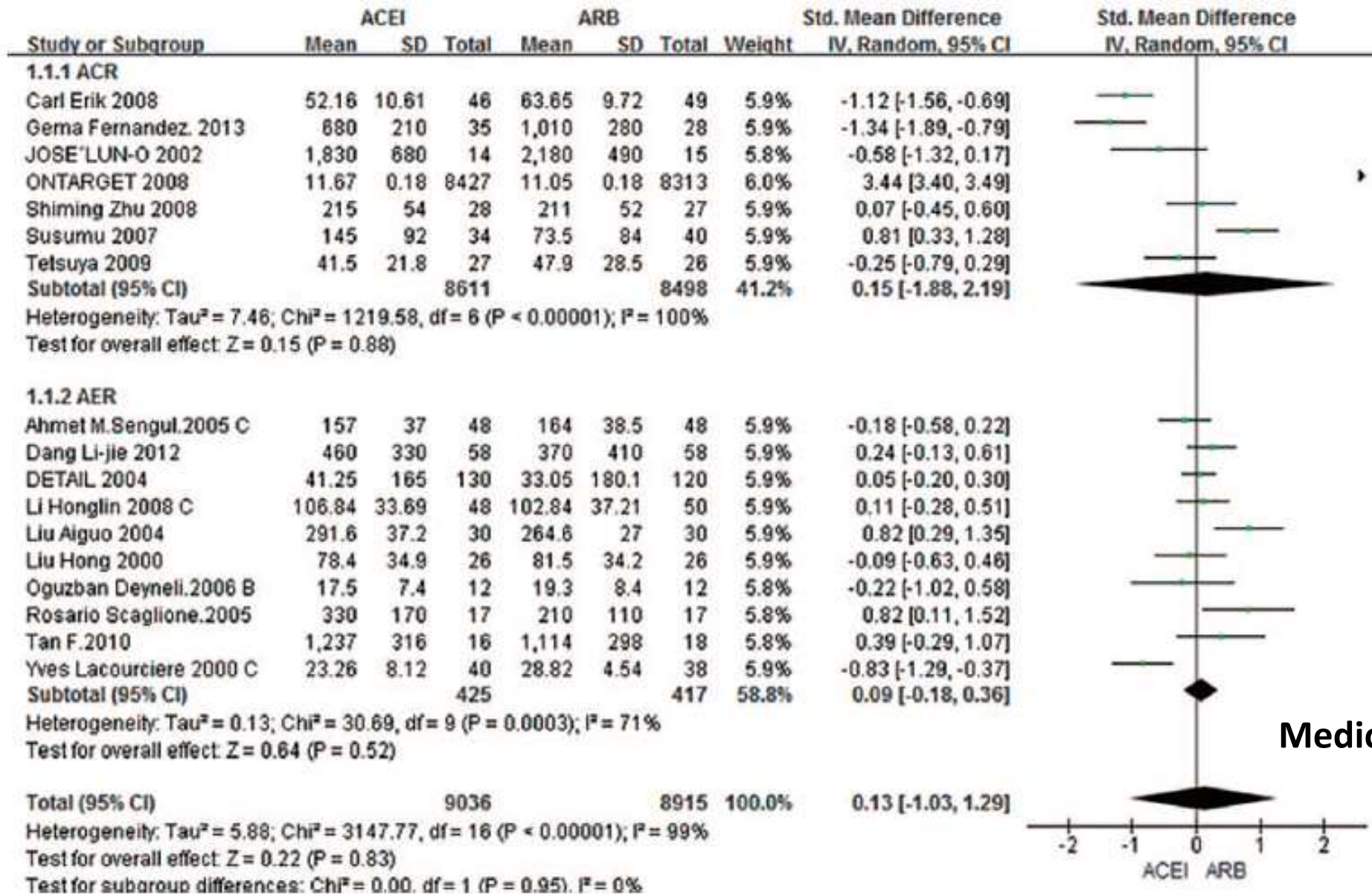
*Rui Xu, MD, Shanmei Sun, MD, Yan Huo, MD, Lin Yun, MD, Shuai Huang, MD,  
Guohua Li, MD, and Suhua Yan, MD*

**Seventeen RCTs, including 17,951 patients**

# Effect on SBP



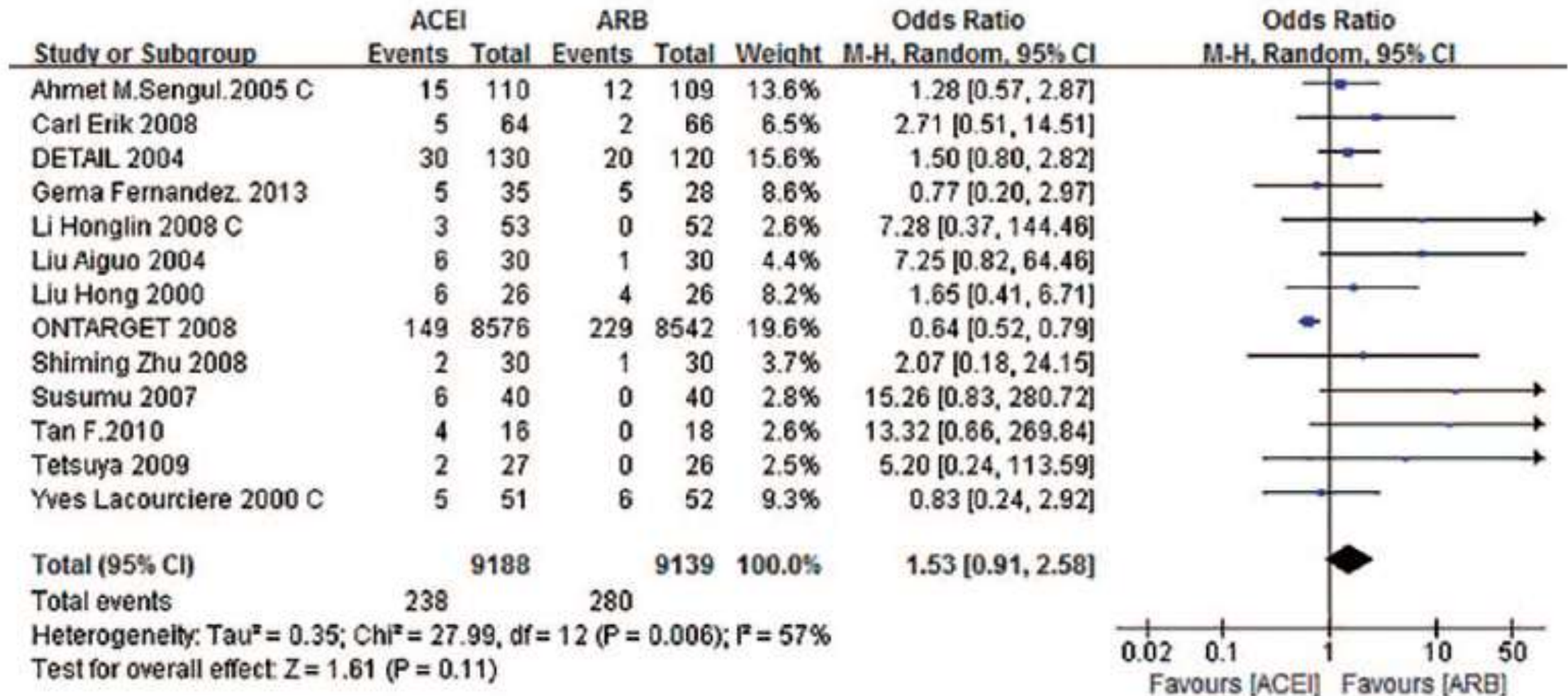
# ACR and AER



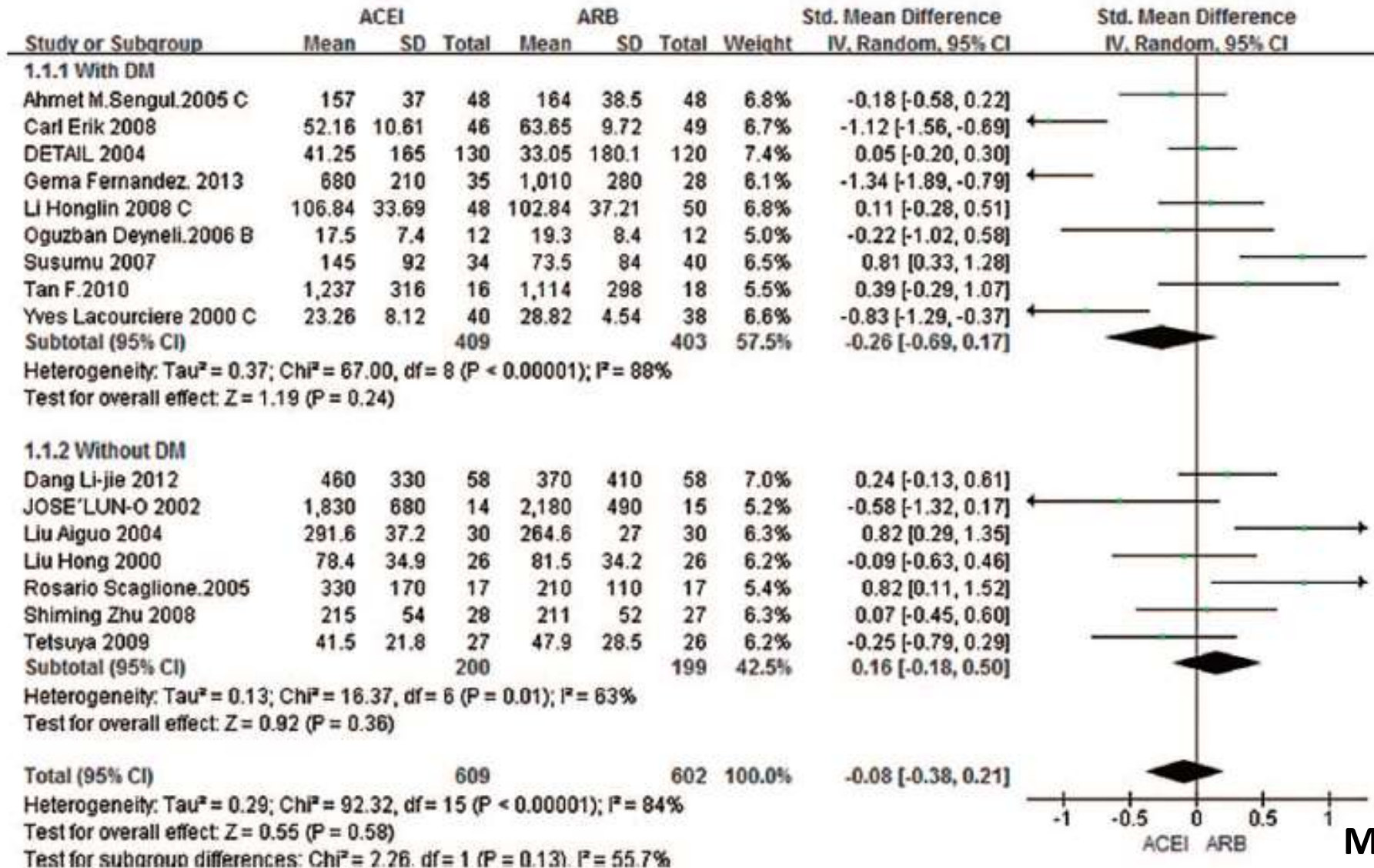
Medicine 2015; 94(39):e1560



# Adverse reactions



# With or without DM



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# Patients without HF



ORIGINAL ARTICLE

## Angiotensin-Converting Enzyme Inhibitors or Angiotensin Receptor Blockers in Patients Without Heart Failure? Insights From 254,301 Patients From Randomized Trials

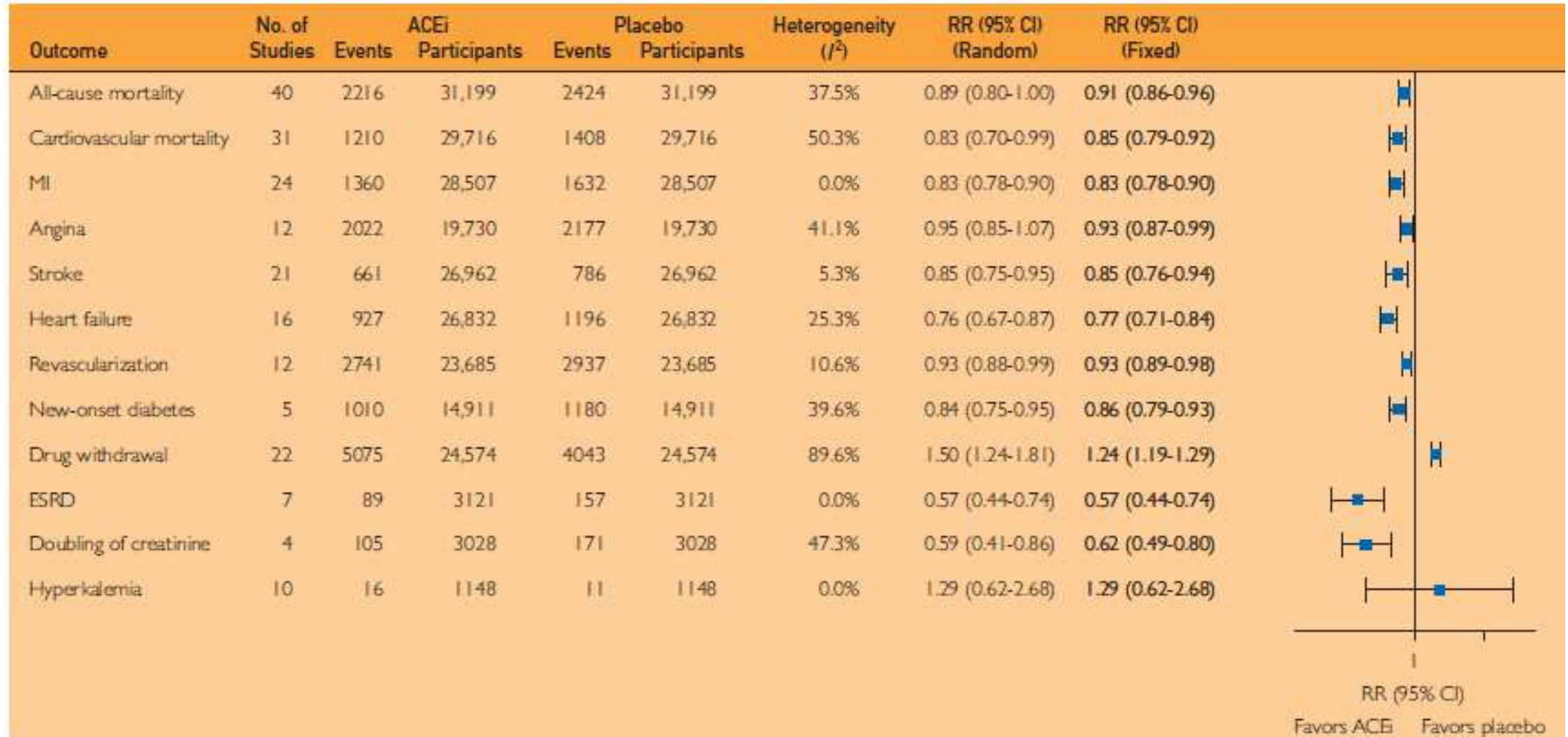


Sripal Bangalore, MD, MHA; Robert Fakheri, MD; Bora Toklu, MD;  
Gbenga Ogedegbe, MD; Howard Weintraub, MD; and Franz H. Messerli, MD

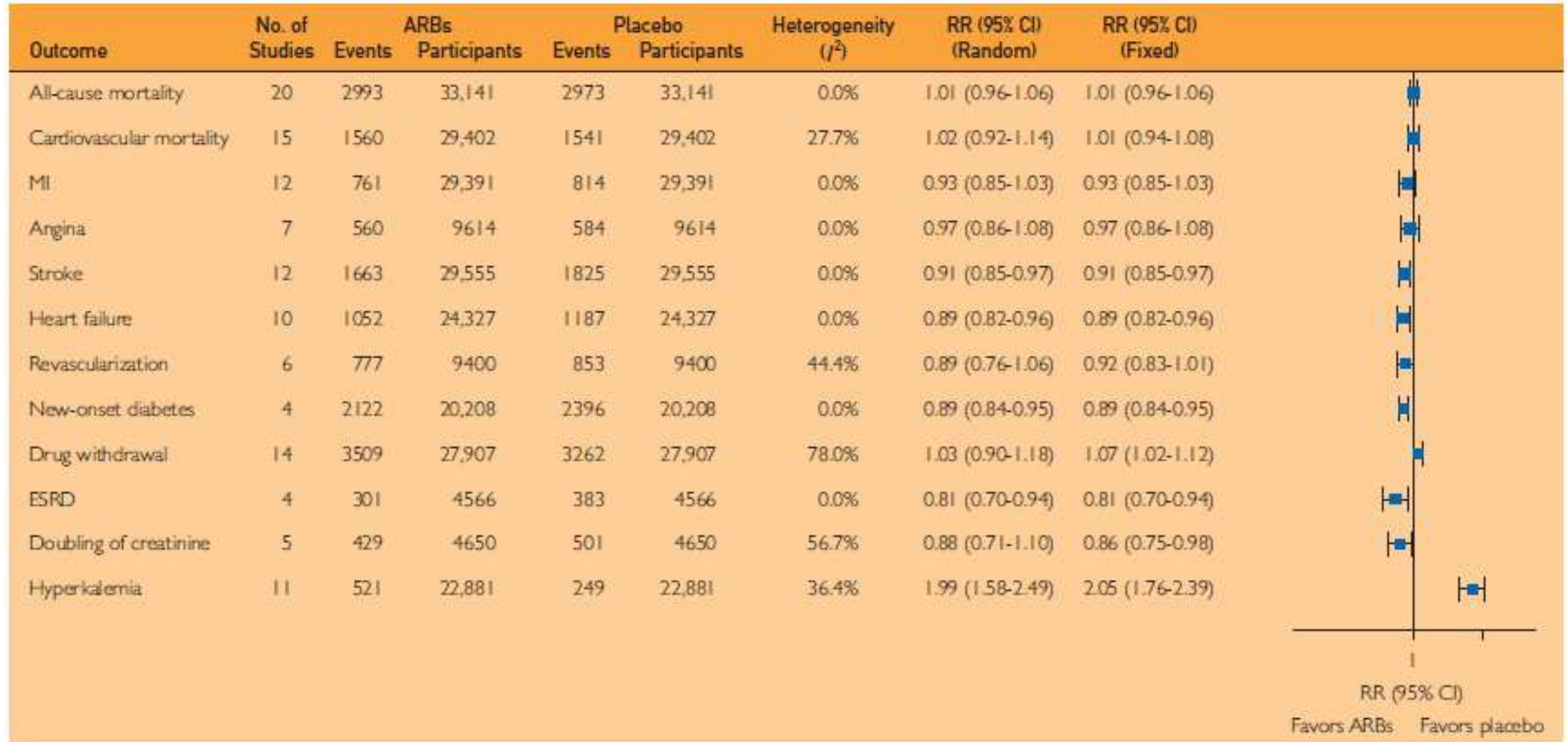
**Mayo Clin Proc. January 2016;91(1):51-60**



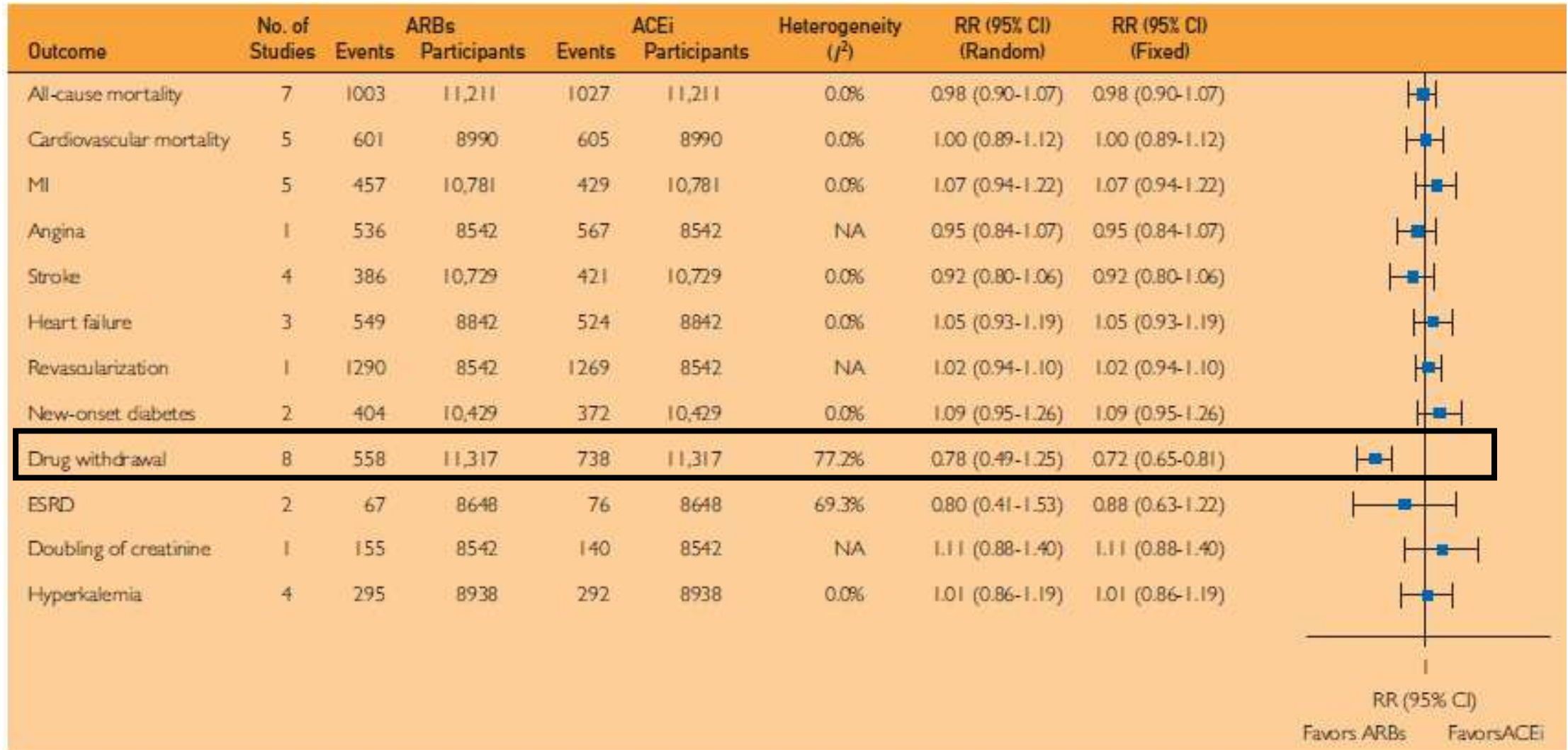
# ACEIS vs placebo



# ARBs vs placebo



# ACEIs vs ARBs



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## After MI

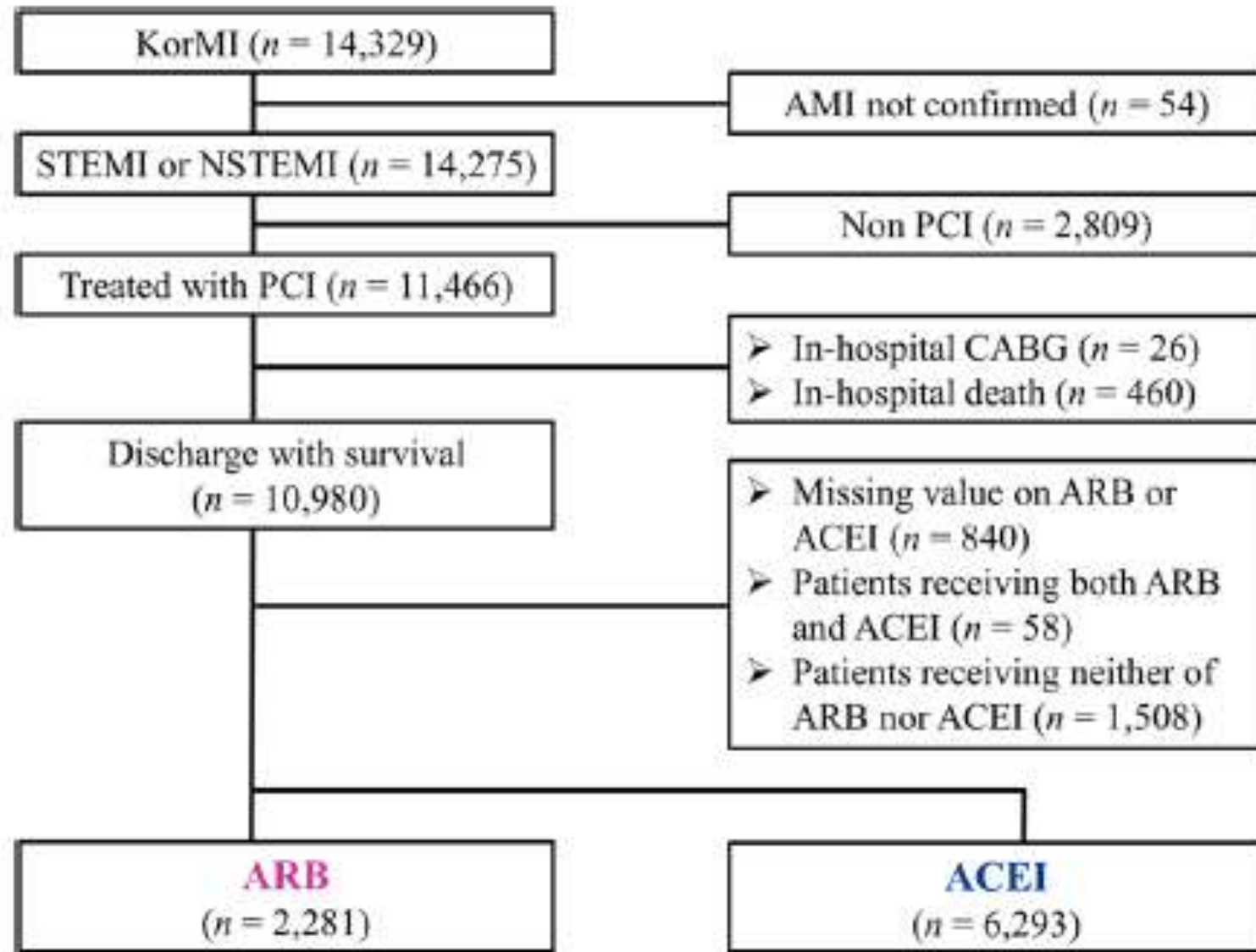
Am J Cardiovasc Drugs (2015) 15:439–449  
DOI 10.1007/s40256-015-0140-5



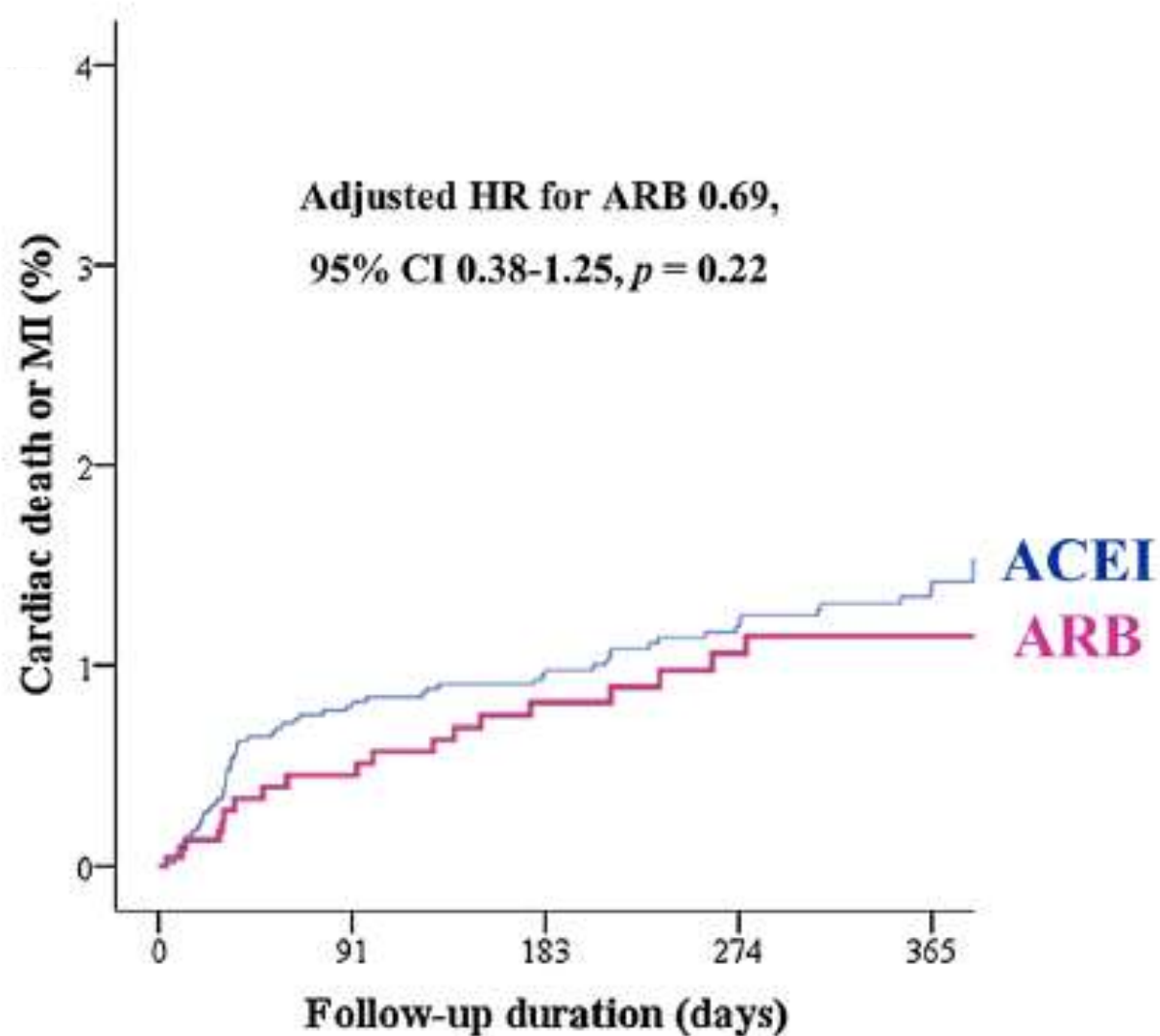
ORIGINAL RESEARCH ARTICLE

### **Comparative Effectiveness of Angiotensin II Receptor Blockers Versus Angiotensin-Converting Enzyme Inhibitors Following Contemporary Treatments in Patients with Acute Myocardial Infarction: Results from the Korean Working Group in Myocardial Infarction (KorMI) Registry**

Pil Sang Song<sup>1</sup> · Sang-Hoon Seol<sup>1</sup> · Guang-Won Seo<sup>1</sup> · Dong-Kie Kim<sup>1</sup> ·  
Ki-Hun Kim<sup>1</sup> · Jeong Hoon Yang<sup>2</sup> · Joo-Yong Hahn<sup>2</sup> · Hyeon-Cheol Gwon<sup>2</sup> ·  
Youngkeun Ahn<sup>3</sup> · Myung Ho Jeong<sup>3</sup> · Young Bin Song<sup>2</sup> · Doo-Il Kim<sup>1</sup> ·  
Other Korean Working Group in Myocardial Infarction (KorMI) Registry Investigators



# Cardiac death or MI





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# Risk of AF and stroke



European Heart Journal  
doi:10.1093/eurheartj/ehs507

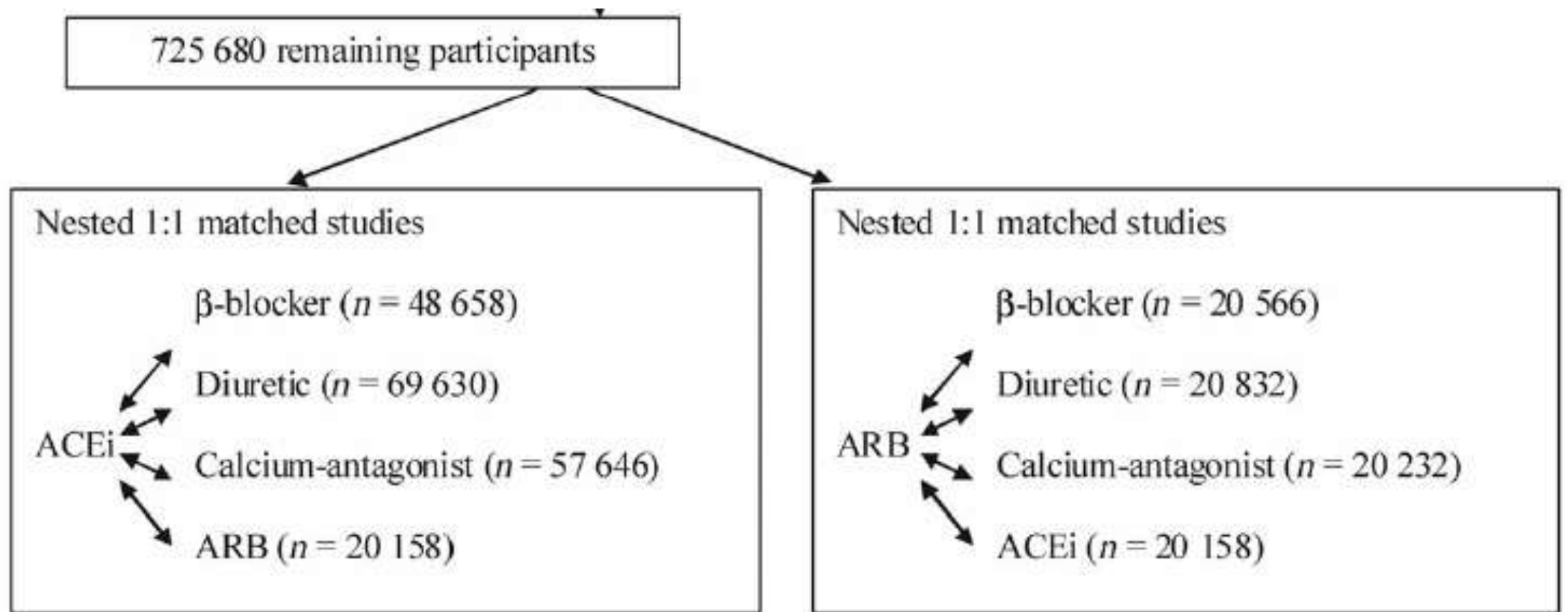
CLINICAL RESEARCH

## Antihypertensive treatment and risk of atrial fibrillation: a nationwide study

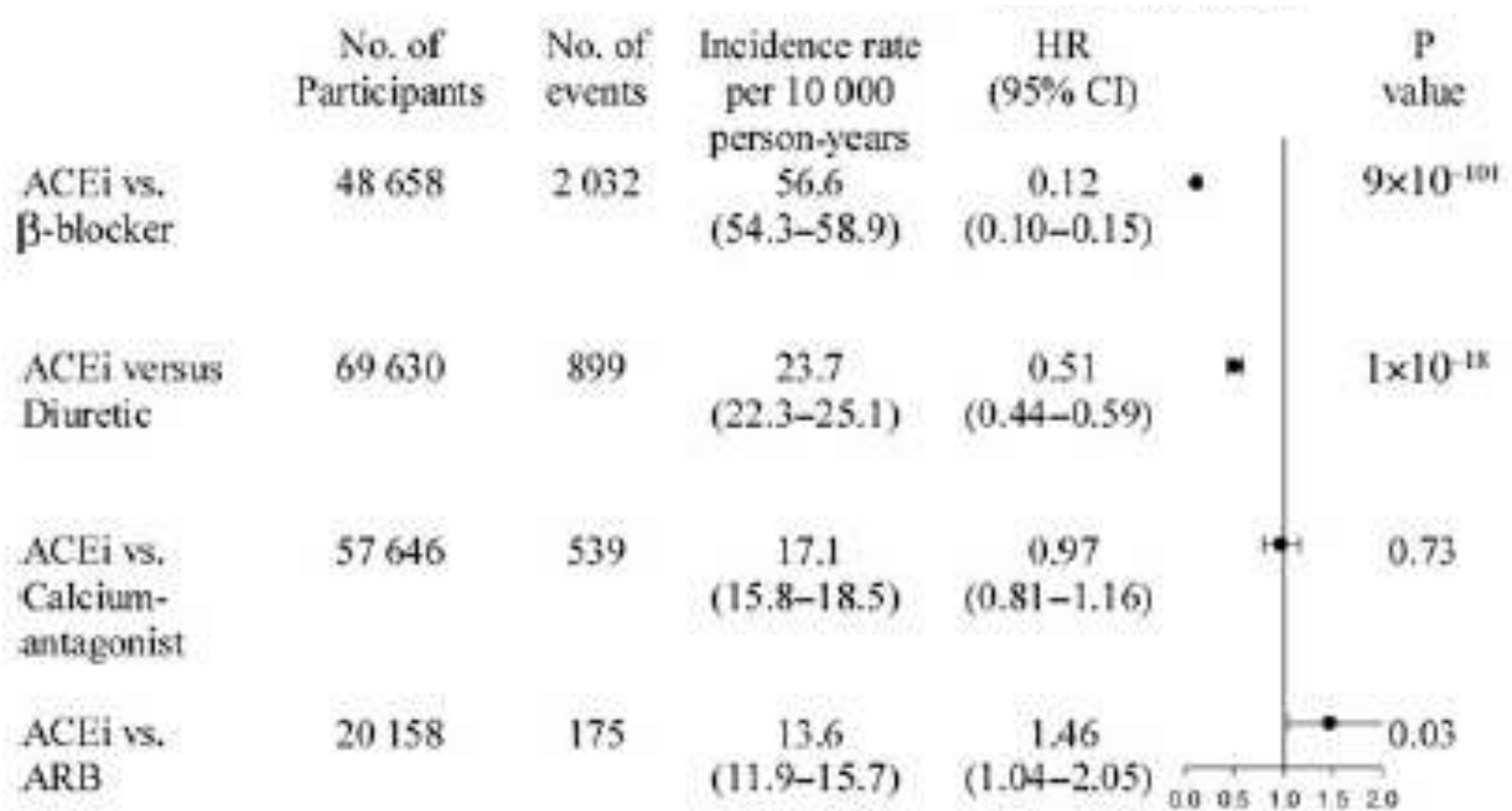
**Sarah C.W. Marott<sup>1,3</sup>, Sune F. Nielsen<sup>1,3</sup>, Marianne Benn<sup>1,2,3</sup>,  
and Børge G. Nordestgaard<sup>1,3\*</sup>**

<sup>1</sup>Department of Clinical Biochemistry, Herlev Hospital, Copenhagen University Hospital, Herlev Ringvej 75, DK-2730 Herlev, Denmark; <sup>2</sup>Department of Clinical Biochemistry, Gentofte Hospital, Niels Andersens Vej 65, 2900 Hellerup, Denmark; and <sup>3</sup>Faculty of Health and Medical Sciences, Copenhagen University Hospital, University of Copenhagen, Blegdamsvej 3B, 2200 Copenhagen N, Denmark

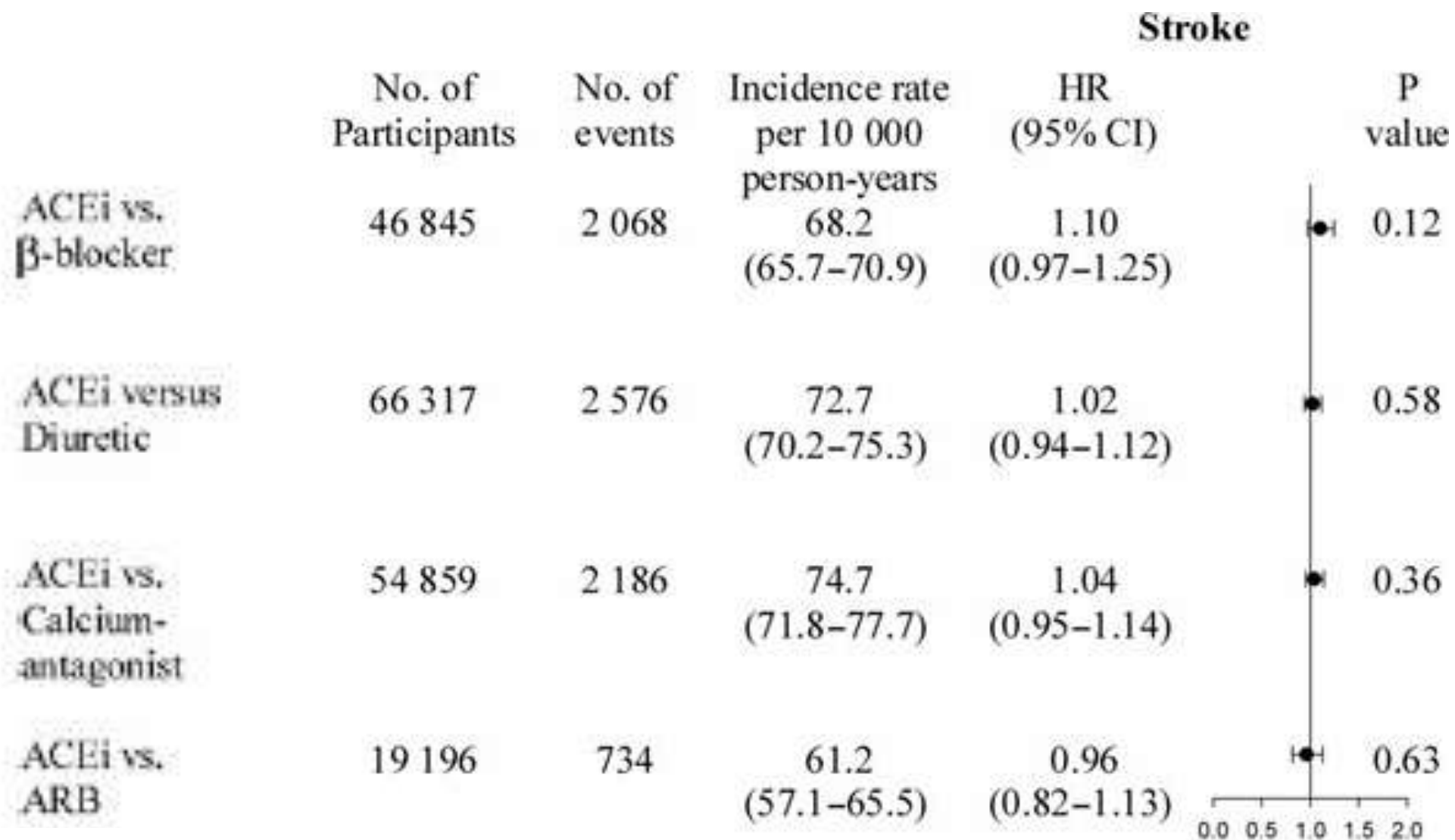
*Received 6 January 2013; revised 7 October 2013; accepted 21 November 2013*



# AF



# Stroke



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  - **CV outcomes in PD patients**

# CV outcomes in PD patients

J Nephrol

DOI 10.1007/s40620-016-0340-3



CrossMark

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ORIGINAL ARTICLE

## **Comparative effectiveness of angiotensin receptor blockers vs. angiotensin-converting enzyme inhibitors on cardiovascular outcomes in patients initiating peritoneal dialysis**

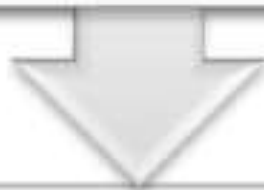
Jenny I. Shen<sup>1,2</sup> · Anjali B. Saxena<sup>2</sup> · Maria E. Montez-Rath<sup>2</sup> · Lynn Leng<sup>1</sup> ·  
Tara I. Chang<sup>2</sup> · Wolfgang C. Winkelmayer<sup>2,3</sup>

Published online: 02 August 2016



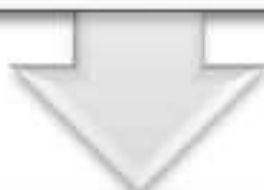
Adult ESKD patients who initiated dialysis from 2007-2011, were stable on peritoneal dialysis by day 90 of dialysis, and had continuous Medicare A, B, & D from day 1-90 of dialysis.

N=4,949



Restrict to patients who filled at least one prescription for an ACEI or ARB during day 1-90 of dialysis.

N=2,063



Exclude patients who filled a prescription for both an ACEI and ARB from day 1-90 of dialysis.

N=1,892

Outcome	Analysis	Exposure group	N	Number of events	Follow-up time (years)		Incidence rate (per 100 person-years)	Hazard ratio (95 % CI)
					Mean $\pm$ SD	Median		
Death, ischemic stroke, or myocardial infarction	ITT	ARB user	741	237	1.55 $\pm$ 1.20	1.25	20.6	0.94 (0.79–1.11)
		ACEI user	1151	387	1.52 $\pm$ 1.17	1.22	22.1	
	AT	ARB user	741	83	0.73 $\pm$ 0.81	0.44	15.2	0.88 (0.66–1.16)
		ACEI user	1151	148	0.73 $\pm$ 0.81	0.45	17.6	
	ITT, $\geq 1$ yr on PD <sup>a</sup>	ARB user	432	127	1.32 $\pm$ 1.00 <sup>b</sup>	1.08 <sup>b</sup>	22.3	0.90 (0.71–1.14)
		ACEI user	662	212	1.27 $\pm$ 1.00 <sup>b</sup>	1.07 <sup>b</sup>	25.2	
All-cause mortality	ITT	ARB user	741	209	1.67 $\pm$ 1.23	1.43	16.9	0.92 (0.76–1.10)
		ACEI user	1151	346	1.64 $\pm$ 1.22	1.33	18.4	
	AT	ARB user	741	65	0.76 $\pm$ 0.84	0.46	11.5	0.81 (0.69–1.11)
		ACEI user	1151	123	0.75 $\pm$ 0.82	0.46	14.2	
	ITT, $\geq 1$ yr on PD <sup>a</sup>	ARB user	464	128	1.38 $\pm$ 1.00 <sup>b</sup>	1.16 <sup>b</sup>	20.0	0.94 (0.75–1.19)
		ACEI user	701	204	1.36 $\pm$ 1.00 <sup>b</sup>	1.20 <sup>b</sup>	21.4	
Cardiovascular death	ITT	ARB user	741	88	1.67 $\pm$ 1.23	1.43	7.1	1.06 (0.80–1.41)
		ACEI user	1151	126	1.64 $\pm$ 1.22	1.33	6.7	
	AT	ARB user	741	31	0.76 $\pm$ 0.84	0.46	5.5	0.97 (0.61–1.55)
		ACEI user	1151	48	0.75 $\pm$ 0.82	0.46	5.5	
	ITT, $\geq 1$ yr on PD <sup>a</sup>	ARB user	464	51	1.38 $\pm$ 1.01 <sup>b</sup>	1.11 <sup>b</sup>	8.0	1.13 (0.78–1.66)
		ACEI user	701	68	1.36 $\pm$ 1.01 <sup>b</sup>	1.19 <sup>b</sup>	7.1	

**Thank You**